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VOL. XV. Nos. 1 and 2 MARCH 18TH AND MAY 20TH, 1921

STORAGE

TRANSACTIONS

OF

THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE

London:
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE
11 CHANDOS STREET, CAVENDISH SQUARE, W.

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ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.

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VOLUME XV. NOS. 1 AND 2.

Proceedings of a Laboratory Meeting of the Society held, by the kind invitation of the Commandant, at the Royal Army Medical College, Grosvenor Road, S.W. 1, on Friday, March 18th, 1921, at 8.15 p.m.

LABORATORY MEETING.

Lieut.-Colonel S. P. LELEAN gave a demonstration of exhibits from the Museum of the Hygiene Department, R.A.M. College, showing methods suitable for tropical hygiene as regards urinals, latrines, incinerators, destruction of insects, trapping of mosquito larvæ, bathing, water cooling and cold storage of food, and disinfection and disinfestation.

Lieut.-Colonel J. C. KENNEDY showed a series of sections of oriental sore, illustrating its histological characters :—

(1) The formation of a tumour the cells of which are heavily infected with *Leishmania tropica*.

(2) The tumour cells in the centre of the growth have the appearance of fibroblasts, but are probably of endothelial origin.

(3) Portions of the tumour show giant cell formation.

(4) The tumour is surrounded by and in parts infiltrated with small round cells and plasma cells.

(5) The tumour extending along the routes of lymph vessels.

(6) Hæmorrhage into the apex of the tumour, with atrophy and gradual erosion of the epidermis.

Lieut.-Colonel H. MARRIAN PERRY gave a demonstration of a helminthic infection in relation to bacterial invasion of the tissues. He remarked that attention was first directed by WEINBERG to the occurrence of bacillary invasion of the tissues in infestations of monkeys with *Œsophagostomum apiostomum*.

The present demonstration is concerned with somewhat similar pathological lesions associated with the presence of another helminthic parasite, *Galoncus perniciosus*.

The animal from which the material is derived was a leopard, *Felis nebulosa*, which died recently in the Zoological Gardens with symptoms of a hæmorrhagic enteritis simulating dysentery. Subsequent examination, however, determined the fact that the condition resulted from infestation with a helminth, *G. perniciosus*, and that death was occasioned by a septicæmia following bacterial invasion of the tissues in the neighbourhood of the parasites.

G. perniciosus is a small nematode worm, which has been encountered on several occasions in the intestine of many of the Felidæ. The worms are found encysted in small nodules in the submucous coat of the large intestine ; some of these nodules are closed, whilst others present a small opening into the lumen of the bowel. In each nodule one or several worms are found lying in a mass of extravasated blood and inflamed tissue.

The pathological lesions are analogous, as noted above, to those observed in infections of monkeys with *Œ. apiostomum*, and the bacterial invasion of the tissues occurs in a very similar manner.

The contents of the submucous cysts become invaded by organisms which may cause a generalised peritonitis by rupture of a cyst into the peritoneal cavity, or a septicæmia by invasion of the blood-stream.

In the case at present under consideration, a bacterial invasion of the blood-stream was the result of the helminth infection.

Bacillus coli and Streptococci of the fæcal type were recovered from the heart-blood, spleen and mesenteric glands of the animal.

The following specimens were demonstrated :—

(1) Ileocæcal junction showing nodules caused by the presence of the helminths.

(2) Thick section of submucous nodule showing three helminths lying in a mass of extravasated blood.

(3) Section of nodule demonstrating spread of bacillary invasion from neighbourhood of helminth.

(4) Section of submucous tissue of cæcum, with masses of hæmatoidin crystals surrounded by a zone of bacterial infection.

Major F. R. COPPINGER demonstrated a method by which he and Capt. R. C. ROBERTSON had prepared a detoxicated vaccine for *B. dysenteriæ*, SHIGA :—

The various stages of preparation and results obtained with rabbits were shown.

The vaccine was prepared by treating the bacilli with strong ammonia and then neutralising with sulphuric acid. The ammonium sulphate formed helped to bring down the altered bacilli in a heavy flocculent precipitate, which, when washed and suspended in saline, formed the vaccine.

It was noted that the bacilli were not broken up or dissolved by this process, as in the case of THOMSON'S detoxicated vaccines ; the only change noted microscopically being a swelling and distortion of their bodies.

Charts, demonstrating the effect of injecting various doses of this vaccine into rabbits, were shown, from which it appeared that the toxicity of the bacilli was considerably reduced, while their power of producing immunity was not appreciably altered. A prolonged series of human experiments is necessary before a definite conclusion as to the value of this vaccine can be obtained.

Professor J. W. W. STEPHENS sent the following exhibits :—

(1) Photographs of claw hand of a patient suspected to be a case of leprosy. No bacilli had, however, been demonstrated in a portion of the thickened internal cutaneous nerve removed at operation.

(2) Four cases of Ainhum toe:—

(*a*) A very early condition.

(*b*) Groove well marked, with outward rotation of the toe and atrophy of the nail.

(*c*) Spontaneous amputation, a condition which was bilateral.

(*d*) Involvement of the fourth and fifth toes in a Kroo-man. Here, again, the condition was bilateral.

Professor WARRINGTON YORKE sent specimens illustrating the development *in vitro* of *Strongyloides stercoralis*.

Dr. PHILIP MANSON-BAHR showed a series of sections of kidneys and spleens illustrating the pathology of a septicæmia, or pyæmia, due to *Bacillus coli*. This very grave disease, attended by a high mortality rate, occurred amongst Turkish prisoners in Egypt during 1916. Seventeen cases had been studied and nine autopsies performed. The clinical and pathological studies based upon the material have already been published in the *Lancet*, in 1918, vol. 2.

At autopsy the kidneys were found to be much enlarged, weighing as much as 14 oz. each; the cortex was studded with numerous small yellow abscesses originating from the Malpighian corpuscles. Secondary abscesses were also found in the spleen and liver. In microscopic sections it was possible to trace the path of the colon bacilli with great nicety. Large aggregations of these organisms could be demonstrated in the intertubular veins, whence they penetrated through the epithelium of the collecting tubules, gaining access to their lumen, and subsequently appearing in the urine.

From a clinical point of view these cases presented a very puzzling appearance. At first sight, some were apt to be mistaken for enteric fever; others suffered from severe recurrent rigors, which much resembled those of malaria in their duration and general course. It was possible to isolate the bacillus from the blood-stream only during the rigors but not during the quiescent periods.

In some cases there were symptoms referable to the urinary system, such as loin pains and frequency of micturition; in others these were completely absent. The urine itself presented a normal appearance, and neither albumen nor abnormal cells were present. The appearance of the bacillus in the urine was also intermittent, so that in order to

diagnose this condition with certainty the urine had to be examined on several different occasions.

The classification of these bacilli was a difficult matter. It was possible to subdivide them on their sugar reactions into several sub-varieties, but there appeared to be nothing attained in doing so, for their pathological effects upon man and laboratory animals in each case were the same.

The entry of the bacillus into the blood-stream would appear to take place through a breach of surface in the intestinal canal; in these prisoners infection appeared to take place through old dysenteric ulcerations of the large gut.

In addition to *B. coli*, septicæmias and pyæmias due to *B. pyocyaneus* were encountered, and microscopic sections were exhibited of one case from which this organism was isolated in pure culture from renal and prostatic abscesses.

The debilitated condition of these subjects predisposed to secondary infections of all kinds, and a slide was exhibited of pneumococci ingested by a polymorphonuclear leucocyte in the peripheral blood from a case of pneumococcal septicæmia. This case was diagnosed while the film was being examined for malarial parasites.

Miss E. M. Baxter and Dr. A. J. Eagleton gave a demonstration of the degree of sterilisation produced by hot oil. It was pointed out that the use of oil for sterilisation of syringes is at present very general. Sir Almroth Wright described a technique for the laboratory and the field, and states that "a temperature of 125° C. to 140° C. will sterilise instantaneously everything with which it comes in contact."[1] Professors Dreyer and Ainley Walker concluded, from a series of experiments, that a temperature of from 150° C. to 170° C. for not less than half an hour is necessary.[2] More recently, Dr. Waterhouse[3] has claimed that the method is valuable.

The importance of the subject is very great, especially to workers in outlying districts who need a simple and efficient method of sterilising syringes. The stress laid on the dangers of quinine injection in the tropics is familiar to everyone.

Four types of experiments have been carried out :—

(1) Subjection of sporing *B. subtilis* to liquid paraffin and olive oil at different temperatures.

(2) Infection of syringes (all glass) with *B. subtilis* cultures. Olive oil and linseed oil and liquid paraffin, at different temperatures, were drawn up and ejected a given number of times. The syringes were then used for transferring sterile broth to sterile broth-bottles.

(3) As in (2), except that the syringes were dried after infection.

(4) As in (2) and (3), except that glass pipettes replaced the syringes.

Controls were done to check the technique.

The experiments, details of which were given, demonstrate that syringes cannot be disinfected by drawing up linseed oil, olive oil, or liquid paraffin five times, even at a temperature of 200° C., and confirm essentially the results of DREYER and AINLEY WALKER.

REFERENCES.

1. *The Technique of the Teat and Capillary Glass Tube.* Sir ALMROTH WRIGHT.
2. *The Resistance of Micro-organisms suspended in Glycerine or Oil to the Sterilising Action of Heat.* PATHOLOGICAL SOCIETY, July, 1912.
3. *B.M.J.* Aug. 2nd, 1919.

Mr. CECIL A. HOARE gave a demonstration on the occurrence of trypanosomiasis in the British sheep. He pointed out that a trypanosome in a British sheep was first observed by WOODCOCK in 1910. He only saw one trypanosome and, unfortunately, gave no description of it. In the following year a similar finding was recorded by BEHN in Germany. On *a priori* grounds WOODCOCK suggested that the trypanosomes in sheep were derived from the flagellates of the sheep-ked, *Melophagus ovinus*, which is a blood-sucking ectoparasite peculiar to sheep, and is nearly always infected with a flagellate known as *Crithidia melophagia*.

A fair number of works dealing with *C. melophagia* and its probable relation to trypanosomes in sheep have appeared, the majority treating this flagellate as a specific insect parasite. Thus, SWINGLE (1911) recorded a series of experiments which he had carried out with the object of establishing the relationship of the ked flagellate to a trypanosome of sheep. He was unable to infect sheep with the ked flagellate, nor did he find any evidence of trypanosomes occurring naturally in sheep.

Last summer Mr. HOARE started working on this question at the suggestion of Dr. C. M. WENYON. While this work was in progress, there came to hand several publications by NÖLLER, who, it appears, had been working on the same subject in Germany, and had already succeeded in finding trypanosomes in sheep by cultural methods.

By using the same methods Mr. HOARE succeeded in cultivating the trypanosomes from sheep's blood, and, by subcultivating in different media, he has already kept cultures alive for more than a month.

In the primary blood cultures the trypanosomes appear after about eight days. They are then typically trypaniform in character, but the kinetoplasts in many already occupy an anteronuclear position; whilst a number show a posteronuclear arrangement of the kinetoplast as in true trypanosomes. In the subcultures the flagellates are of a typical Crithidia form and quite indistinguishable from those found in the sheep ked. All these types will be found under the microscopes.

The reason why so many investigators failed to find trypanosomes in sheep is accounted for by the very scanty number present in the blood. Mr. HOARE has examined a series of thick blood films from thirty-five sheep—a great number of which were proved by culture to be infected—without finding a single trypanosome.

There can be no doubt that the sheep become infected from the sheep-ked, which thus becomes the intermediate host of the sheep trypanosome, which now bears the name *Trypanosoma melophagium* (=*Crithidia melophagia*).

This trypanosome is, as far as is known, a harmless parasite, but it must be borne in mind that there are several diseases of unknown nature in sheep, which may prove to be due to this trypanosome.

The investigation is still in progress, and Mr. HOARE hopes to be able to test the question of transmission and pathogenicity later on.

The following preparations were shown :—

(1) Live trypanosomes from subculture.

(2, 3, 4) Stained preparations of trypanosomes from cultures.

(5, 6) Preparations showing gradation forms (from trypanosomes to crithidia).

(7, 8) Crithidia forms from the sheep (from culture).

(9, 10) Crithidia forms from the gut of the sheep-ked.

(11) Leishmania and pear-shaped forms from the rectum of the sheep-ked.

(12) Section of the gut of the sheep-ked showing flagellates attached to the wall.

(13) The intermediate host of the sheep-trypanosome, the sheep-ked (*Melophagus ovinus*).

Dr. R. St. John Brooks showed the following preparations and cultures:—

(1) Microscopical demonstration of slide preparations of *Leptospira icteroides* and *Leptospira icterohæmorrhagiæ.*

(2) Cultures of micro-organisms illustrative of tropical bacteriology:—

Typhoid and paratyphoid fever: salmonellosis, including paratyphosus C, and various types of suipestifer.

Bacillary dysentery: Flexner types (including monkey strains) and Shiga.

Hæmorrhagic septicæmia group: *B. pestis*, *B. pseudotuberculosis rodentium* and Pasteurellas from rabbits, cattle, sheep and pigs.

Malta fever and abortion of cattle, including Feusier and Meyer's types of *B. abortus* and *B. melitensis.*

Acid-fast bacteria including various organisms isolated from leprous lesions, *B. tuberculosis* (human, bovine and avian) and Johne's bacillus.

Vibrios: V. choleræ, V. El Tor, V. para-cholera A and B (Mackie and Storer), and cholera-like vibrio from water.

Skin fungi: epidermophyton, trichophyton, etc,

Blastomyces: streptothrix, sporothrix, etc.

Blastomyces and torulæ from lesions from man and horses, *Coccidiodes immitis* from case of San Joaquin Valley disease (Coccidioidal granuloma), sporothrices from man and horses, streptothrix from camel, and Nocardia from eye disease, Khartum.

Eastern Fermentation Industries:—

Moulds from Saké, etc.: *Aspergillus oryzæ*, *Rhizopus Japonicus* and *Mucor* (*Amylomyces*) *Rouxii.*

Yeast from African millet beer (Pombé); Schizosaccharomyces (Pombé).

Yeast from Kefir: *Saccharomyces fragilis* and "Kefir" yeast (Hansen).

Sauces and pickles: *Saccharomyces farinosus* and *Aspergillus tamari.*

Dr. C. M. Wenyon gave a demonstration of preparations illustrating:—

(1) The structure of Trichomonas and its invasion of the tissues of the intestinal wall of human beings and rats.

(2) The hæmogregarine (*Hepatozoon canis*) of the leucocytes of the

dog, showing the blood form, the schizogony stage in the spleen, and the oöcyst in the tick *Rhipicephalus sanguineus.*

(3) The hæmogregarine (*H. muris*) of the leucocytes of the rat, showing the blood form, the schizogony stage in the liver, and the oöcyst in the mite *Lelaps echidninus.*

Drs. J. G. Thomson and A. Robertson gave a demonstration illustrating the frequent occurrence of Charcot-Leyden crystals in the fæces of amœbic dysentery cases, and pointed out the value of these crystals as an aid to the diagnosis of such cases. The following specimens were shown:—

(1) A Charcot-Leyden crystal in the cytoplasm of a free *Entamœba histolytica.*

(2) Charcot-Leyden crystals from a sigmoidoscope scraping of an amœbic ulcer. Numerous small crystals arranged in clumps.

(3) Charcot-Leyden crystals from a sigmoidoscope scraping of an amœbic ulcer, showing several large crystals.

(4) Free *E. histolytica* along with Charcot-Leyden crystals in the same microscopic field from the blood and mucus of an amœbic infection.

(5) Charcot-Leyden crystals associated with the cysts of *E. histolytica.*

Nos. 1, 2, 3 and 5 stained with Heidenhain's Iron Hæmatoxylin; No. 4 stained with Ehrlich's Acid Hæmatoxylin and Eosin.

Microphotographs and camera-lucida drawings of Charcot-Leyden crystals in their relationship to *E. histolytica* were also shown.

Dr. A. Castellani showed specimens illustrating the identification of sugars by the mycological method.

Proceedings of a meeting of the Society held on Friday, May 20th, 1921, at 8.45 p.m., at 11, Chandos Street, Cavendish Square, W. 1, Professor W. J. R. Simpson, C.M.G., M.D., F.R.C.P. *(President)*, in the Chair.

A NEW METHOD OF TREATMENT OF TRYPANOSOMIASIS.

BY

CLAUDE H. MARSHALL, M.R.C.S., L.R.C.P., *S.M.O. Uganda Protectorate.*

I have very kindly been allowed to read to you to-night a paper on a new method of treatment of trypanosomiasis which has been originated by Dr. S. M. Vassallo of the Uganda Medical Service and myself.

Sleeping sickness depends for its causation on three factors, namely, (1) the human host, (2) Glossina (tsetse-fly), and (3) the trypanosome; any two of these are harmless in the absence of the third, so that in dealing with this disease we have three different courses open to us:—

(*a*) Human beings may be excluded from areas infected by the Glossina;

(*b*) The fly may be driven away by depriving it of its shelter and food; and

(*c*) attempts may be made to cure infected persons.

The first course (*a*) has been that most employed, and is the only one which has been generally successful in preventing the incidence of sleeping sickness. It amounts, however, to nothing more or less than surrender to the tsetse-fly, and, as a result, enormous areas of country have been evacuated and abandoned. (*b*) During the past ten years something has been done to stamp out the tsetse-fly by destroying its breeding-grounds, driving away its food supply, and cutting down the bush which forms its natural shelter. (*c*) Attempts to cure patients infected with the trypanosome have, in the vast majority of cases, proved unsuccessful, although individuals—certainly European and Asiatic, possibly also African—have recovered, but, taken generally, sleeping sickness must still be regarded as a fatal disease. Although many drugs cause a marked temporary improvement, each falls short of certainty in effecting a cure.

Most authorities are agreed that the administration of one dose of salvarsan, neo-salvarsan or atoxyl is sufficient to sterilise the blood-stream, but within a variable period, averaging about four months, the symptoms reappear, and the disease progresses to a fatal termination.

Excluding reinfection, two theories have been put forward by other workers to account for this, namely, (1) that the trypanosome assumes a resistant form and becomes what is known as "atoxyl fast," or (2) that some of the parasites are protected from the action of the drug by assuming a secluded position in the central nervous system.

That the second of these theories is the right one is, I think, proved by the following cases:—

Case 7.—A man with a few small glands in his neck was found to have trypanosomes in his gland-juice on June 1st, and again on July 1st, 1919. On July 10th, he was given an intravenous injection of 0·6 gms. of neo-kharsivan. On July 27th, his glands were smaller and harder, and no trypanosomes could be found in them; nevertheless, on October 28th, three and a half months after the injection of neo-kharsivan, living trypanosomes were found in the cerebro-spinal fluid.

Case 30.—A man with large typical chains of glands in the neck had numerous trypanosomes in the gland-juice on June 14th, 1920;

0·6 gms of neo-kharsivan were injected into a vein, and three days later living trypanosomes were found in his cerebro-spinal fluid. Again, in Case 33 living trypanosomes were found in the cerebro-spinal fluid three days after an intravenous injection of neo-kharsivan.

In Case 34, there were trypanosomes in the gland juice on the 3rd August, 1920, and the man was given the usual intravenous injection of neo-kharsivan. Living trypanosomes were found in his cerebro-spinal fluid three months afterwards, though nothing abnormal could be found by repeated examination of his blood and gland-juice, either then or at the end of November.

In these four cases the blood and gland-juice were rendered free from parasites, presumably by the intravenous injection, but in both as early as three days, and as late as three and a half months afterwards, living trypanosomes were found in the cerebro-spinal fluid.

VASSALLO has found, in performing post-mortem examinations on one or two fatal cases of sleeping sickness, that the meninges of the brain are greatly thickened, and we suggest that the action of the trypanosome in the central nervous system is to cause such thickening of the membranes that the connection between the blood-stream and the cerebro-spinal fluid through the choroid plexus is occluded quite early in the disease, and that, as a result, drugs circulating in the blood-stream are not eliminated into the spinal fluid, so that when the trypanosomes in the blood are killed off by natural, or artificial means, the infection persists in the central nervous system, later on, may be, to reinfect the blood-stream again. On this point Professor KEITH has very kindly furnished me with the benefit of his views, and he states: "While the exact anatomy of the route is unknown, there is no doubt that infections in the basal cisterns do reach the cervical glands, and that very probably this occurs through the nerve-sheaths, where there is some connection between the cerebro-spinal and the lymphatic systems." On this assumption, the trypanosome is protected by its position in the body and its suggested resistance to atoxyl and similar preparations is not proved, inasmuch as the trypanosome would not be brought into actual contact with the drug.

In the treatment of sleeping sickness, therefore, two separate foci of infection must be considered: the initial infection of the blood-stream, causing fever, skin rashes, etc., from which the patient recovers, either

with or without treatment, and the second focus in the cerebro-spinal fluid, where the trypanosomes cause cerebro-spinal lesions leading to the death of the patient.

Before the cerebro-spinal fluid has been invaded, there appears to be no reason why injections of arsenic and other preparations should not cure the patient; but once the invasion of the central nervous system has occurred, and drugs can no longer reach it from the blood-stream, all intravenous medication is useless, except to deal with such parasites as subsequently reappear in the blood-stream from the lymphatic system.

In the autumn of 1918, on the supposition that the above theory offered an explanation as to why all forms of treatment hitherto had proved so unsuccessful, I attempted intrathecal, in addition to intravenous medication.

My first case was a man with small typical glands (harbouring trypanosomes) in the neck, who was injected with 0·6 gms. of neo-kharsivan intravenously on September 26th, 1918. Three days later, 0·025 gms. of neo-kharsivan were injected into his spinal canal; he died the following day.

As this form of treatment failed it was not repeated, but the next case (a woman) was given an intravenous injection of neo-kharsivan, and three hours later two ounces of her blood were drawn off into a sterile covered vessel, which was left standing in a bowl of cold water for twenty hours, by which time the clot had separated. Twenty mimims of the clear serum were then injected into her spinal canal, after a corresponding amount of spinal fluid had been drawn off by lumbar puncture.

This woman was a well-marked case of sleeping sickness, trypanosomes being easily found in the large typical glands in the neck, and, though she has had no more treatment of any kind, and has been examined at intervals of three months, her blood has remained negative. When seen in December, 1920, twenty-seven months after treatment, she was quite well. Her blood and cerebro-spinal fluid were then negative, and the glands in the neck, which had completely disappeared soon after the injection, had not reappeared.

Thirteen other cases were treated in the same way. The amount of serum injected and the length of time between the injection of neo-kharsivan and the drawing off of the blood was varied. The results

obtained up to the end of 1919 were published in the *British Medical Journal* of May 22nd, 1920.

In February, 1920, I was relieved by Dr. S. M. VASSALLO, and he took over the patients I had already treated, and, during the past year, has dealt with a number of new cases. The whole are shown in the table :—

TABLE.

Case Number.	Number of months since treatment to Dec., 1920.	Examined December, 1920: Blood.	C.F.S.	Glands.	
2	27	neg.	neg.	disappeared.	Quite well.
3	27				No. records.
4	24	do.	do.	do.	Quite well.
5	18				No records.
7	19	do.	do.	do.	Quite well.
8	16	do.	do.	do.	do.
9					Died; very advanced case.
10					do. do. do.
11	13	do.	do.	do.	Quite well.
12	13	do.	do.	do.	do.
13	13	do.	do.	do.	do.
14	13	do.	do.	one gland neg.	Well.
15	12	do.	do.	disappeared.	Quite well.
16	8	do.	do.	do.	do.
17	8	do.	do.	do.	do.
18	8	do.	do.	do.	do.
19	8	do.	do.	do.	do.
20	8				Not reported for examination. No records.
21	8	do.	do.	do.	do. do. do.
22	8	do.	do.	do.	
23	8	do.	do.	do.	Treated atoxyl; serum; quite well.
24	8	do.	do.	do.	do. do. do.
25	8	do.	do.	do.	do. do. do.
26	7½	do.	do.	do.	Quite well.
27	7½	do.	do.	do.	do.
28	7½	do.	do.	do.	do.
29	7½	do.	do.	do.	do.
30	6½	do.	do.	do.	do.
31	6½	do.	do.	do.	Treated plain serum. Quite well.
32	6½	do.	do.	do.	Quite well.
33					Died after anæsthetic—delayed chloroform poisoning.
34-56	Under six months since treatment and not yet re-examined.				

In this connection I must explain that all work done by both VASSALLO and myself on the subject of sleeping sickness has been in addition to our ordinary duties as District Medical Officers, and, as a

result, several of our records are incomplete. For instance, several cases on the table are marked as "no records." This was owing to the fact that early in 1919 I had to leave my station for over two months to undertake other duties, and during this period a severe famine occurred in the district, causing the death of between 20,000 and 30,000 natives. On my return I could learn nothing of Cases 3 and 5, except that they were reported to have died, but no definite information could be obtained.

Again, Case 10 was discharged to his home and later on was reported to have died. Since he was in an advanced stage of the disease we have presumed that he died of sleeping sickness.

Case 6, omitted from the table, was a dog infected with the *T. gambiense*, or human strain of trypanosome, and was treated as a control to see if an intravenous injection of neo-kharsivan alone would cure the disease, but the animal had to be shot about a month later as being hopelessly ill.

Fifty-six cases are recorded, and fifty-two of these have been treated by some form of serum.

Of these fifty-two, six are dead or presumed dead; practically all the others were seen in December, 1920, and found to be perfectly well. In all cases the blood and cerebro-spinal fluid were examined, with negative results.

As a point of considerable interest, although all these cases originally had well-marked glands, yet after serum treatment these glands have invariably disappeared completely, while in cases not treated by serum the glands remain.

Of the six patients who have died, two disappeared during the famine, and one, at any rate, of these is stated to have died of starvation. Two died of intercurrent disease and two we presume died of sleeping sickness. These last, before they came for treatment, were very advanced cases of the disease, one being unable even to stand.

On the other hand, one case, the woman referred to, has remained quite well after twenty-seven months; another after twenty-four months, and seven more after over a year since being treated by a single dose of serum.

One patient treated in April, 1920, aged about 60, cycled in thirty

miles one morning for re-examination, a notable feat for him, since he stated that he had not been able to ride a bicycle for at least a year before treatment. Three other cases, treated over a year ago, when they admitted to being impotent—indicating involvement of lumbar nerve centres—are no longer so. They have since become fathers. Enough has been said to show that this method of treatment is successful, or, at any rate, certainly gives better results than have hitherto been obtained by other methods of treatment, especially when it is borne in mind that all these cases have had only one dose of serum.

The question, then, arises whether this injection of salvarsanised serum into the spinal canal has given such good results from its antiseptic, or rather antiparasitic, action alone. It appears to us as improbable, if 0·6 gms of neo-kharsivan are dissolved in all the blood in the body, and then 20 minims of this mixture are again diluted by the whole bulk of the cerebro-spinal fluid, that the resulting solution can be powerful enough to kill off the trypanosome.

We suggest that some trypanolytic antibody is normally formed in the blood as a reaction to the invasion by the parasite, and that this effects a natural cure as far as the blood-stream only is concerned. However, since in fact the cerebro-spinal fluid contains no antibodies, opsonins, or alexins, and as we suggest the cerebro-spinal fluid is cut off from the blood-stream by the disease, it follows that a natural cure cannot take in the central nervous system, but injection of blood serum containing the trypanolysin into the spinal canal is sufficient to kill the parasite, either directly or, as Dr. ABADIE of Paris believes, by stimulating the formation of further complements.

To support this theory of trypanolysins we have in several cases given the patient no intravenous injection at all, but have simply drawn off a quantity of blood from a vein (under aseptic conditions) and allowed it to stand for as long as three days; we then injected the serum into the spinal canal, expecting that any contained trypanosomes would have died from exposure and the trypanolysins in the serum would effect the cure of the infection in the cerebro-spinal fluid, at the same time the parasites in the blood-stream would be destroyed by their own antibodies.

The first case so treated (No. 31 male, *æt.* about 30) has now

gone on well for six months up to December, 1920. No trypanosomes could then be found in his blood or spinal fluid; the glands in his neck had disappeared.

Following up this line of treatment, VASSALLO is trying now the effect of the intraspinal injection of serum from a previously treated case into a patient with sleeping sickness. It is, however, yet too soon to form any opinion as to its effect.

Of more interest in this connection is the case of Mr. J. G. Rubie, our only European patient, who has been good enough to come here to-night. He had attacks of what he believed to be malaria, commencing July 30th, 1920, and, finally, had his blood examined on August 24th, when it was found to be swarming with trypanosomes.

I first saw him as a patient on September 24th, 1920. He had general lassitude, malaise, distaste for food, attacks of vomiting, with pains in the back and limbs, and a dull headache. He had lost two stone in weight. There was one small gland in the neck (which may possibly have been septic in origin) and his blood showed two or three trypanosomes in each field.

He was given 0·9 gms. of neo-kharsivan intravenously and 12 c.c. of serum into the spinal canal, the blood being drawn off after half an hour. He showed a very severe reaction for several days and then made uninterrupted recovery. He has lost all symptoms, regained his lost weight, and will, I think, tell you that he feels absolutely well. It is a year since the probable date of infection, and nearly eight months since this single treatment which I have just detailed.

However, on November 2nd, 1920, about six weeks after the injection of serum, while nothing abnormal could be found in his blood, subinoculation on that day into two rats and a monkey resulted in one rat showing trypanosomes on November 30th, while the other rat was negative. The monkey became very sick though it did not die, and no trypanosomes where found in its blood.

At this time, then, Mr. Rubie still harboured the parasite in his system though apparently a strain of a low virulence, since the monkey showed only a mild infection.

On December 21st, 1920, the blood was examined again, both fresh and stained, by Professor J. EYRE, who reported one degenerate trypanosome without a nucleus, the only organism found in eight slides. Sub-

inoculations into two guinea-pigs were negative. One of these guinea-pigs was post-mortemed about six weeks later, and was found absolutely healthy.

Then there arose the question as to what had occurred to account for this history, and three possibilities were considered :—

(1) An error in technique, that is to say, that the dose of neo-kharsivan had been too large or the time between the injection and the drawing off of the blood too short. Professor EYRE suggested that a provocative dose of 0·3 gms. of neo-kharsivan, and a period of one and a half hours before drawing off the blood, would establish the most favourable conditions for the production of trypanolysins, and

(2) That treatment had been commenced too early in the disease, and the body had not had time to react and produce antibodies to the trypanosome, with the result that the serum was valueless. If this were the case, it would, I imagine, be incompatible with the experience of most of us that late rather than early treatment in a progressive disease could be to the patient's advantage, and

(3) That the presence of degenerating trypanosomes in the body after treatment was merely a feature of the normal process of the cure by this method. We accept this as the explanation.

It was decided, in consultation with Dr. PROUT and Professor EYRE, to examine Rubie again, and, if no trypanosomes could be found, to allow matters to take their course without any attempt at further treatment. So, on January 20th, 1921, lumbar puncture was performed and the cerebro-spinal fluid was examined, both fresh and stained, also 1 c.c. each was sub-inoculated into two rats ; all results proved negative and the cerebro-spinal fluid contained no cells of any kind.

The patient was examined again on April 7th, 1921, and his blood found to be negative on examination of fresh and stained slides and sub-inoculation into two rats and six mice. On May 2nd his cerebro-spinal fluid was normal and negative on subinoculation into three rats and two mice.

That Rubie's presumed cure is not due to the initial dose of neo-kharsivan killing off all the trypanosomes in the body is certain, since the sub-inoculation on November 2nd showed that he still harboured the parasite ; that treatment was effective, both in technique and time, is shown by his excellent clinical history and the completely negative

results of microscopical examination and of further sub-inoculations since the beginning of this year. We believe that the explanation of his history is that the injection into the spinal canal dealt with that focus of infection while the continued formation of trypanolysins in the blood gradually destroyed the parasites in the blood-stream.

Our two most advanced cases of sleeping sickness did not prove amenable to treatment, and we are proposing to treat such cases in the future by the injection of serum into the lateral ventricles as well as into the spinal canal, on the supposition that something of the nature of an obstructive hydrocephalus occurs in these patients, through the occlusion of the foramen of Majendie by thickening of the membranes, and that, as a result, intrathecal injections are unable to reach the cavity of the brain. This idea is supported by the fact that often, in advanced cases, no cerebro-spinal fluid at all can be obtained by the lumbar puncture.

We intend, however, to investigate this point by injection of indigo-carmine into the lateral ventricle and endeavouring to recover it by lumbar puncture. Inability to do so would prove the correctness of this theory, and indicate that these cases require serum to be injected directly into the brain cavity.

To sum up, as far as our experiments have gone, they show (1) that there are two distinct foci of infection in an established case of sleeping sickness, and that of these the focus in the central nervous system is the important one, but that this can be dealt with effectively by a single dose of some sort of serum; (2) that the results of such serum treatment in over fifty cases appear to be better than any of the results hitherto obtained by repeated intravenous or subcutaneous injection of salvarsan, atoxyl, antimony or other preparations; and we suggest that the curative effect results from the formation and action of some form of trypanolysin.

If our theories are correct, there appears no reason why animal serum should not be used for treatment, why some degree of prophylaxis and immunity to trypanosomiasis should not be obtained, and why early diagnosis should not be effected by some form of complement fixation test. Upon all these questions VASSALLO is carrying out experiments.

Further, the line of treatment adopted for human beings can probably be applied to animals. The cure of "fly" disease in horses and cattle should prove of great economic value, and, given time and oppor-

tunity, both VASSALLO and I have great hopes of being able to deal simply and effectively with trypanosome diseases both in man and beast. But we are very anxious that we should be assisted by the Veterinary branch of Medical Science in these researches. The problem of trypanosome infection is the same whether applied to human beings or other animals, and experiments on the treatment of each dovetail into one another, so that the co-operation of a veterinary officer in future work is extremely desirable.

DISCUSSION.

The PRESIDENT: This is the second paper we have had on trypanosomiasis this session. The first was by Professor WARRINGTON YORKE, who raised a very lively discussion in this room because of his criticism of the proposal to spend £30,000 on trypanosomiasis investigation from the zoological side. It was felt at the time that a research of this kind would be extremely valuable, but that it was somewhat limited in scope, and that there were other aspects of the question which required attention; for instance, there were the medical, the veterinary, the laboratory, the administrative and other sides. To-night we have had the medical side put to us, and it is a very important one. I consider that this paper is one of the most important that have been placed before this Society. If the results which have been told us to-night are maintained in the future, and are confirmed by further investigations, they indicate, to my mind, a new and brilliant era in the treatment and prevention of trypanosomiasis.

What does that mean to Africa? I have only to bring to your minds the vast area of Africa infested with the tsetse-fly, the scourge which trypanosomiasis has been to the African population, and the ever-present danger of this disease spreading. These conditions present a great and perplexing problem, and I think that any researches that may be placed before this Society which in any way contribute to a solution of this subject are particularly welcome. I place in this category the paper which has just been read. These experimental observations of Dr. VASSALLO and Dr. MARSHALL have not been made on the lower animals, but they have been on men and women, and the results, so far as they go, certainly appear to me to hold out a reasonable prospect of a reduction in the mortality and the dangers of, at least, one of the forms of trypanosomiasis.

In presenting his statement to us, Dr. MARSHALL has, very rightly, excluded the twenty-three cases that were treated only six months previously. This leaves thirty-one cases, and one of these thirty-one died under chloroform, so that it can hardly be counted. If we take this group of thirty cases which has been treated by the serum only once, and more than six months ago, we find that twenty-two cases are still alive and well; that is to say, that 73 per cent. of the cases that have been so treated are alive and well after six and a half months and more. If we analyse Dr. MARSHALL'S table further, we shall find that thirteen cases were treated a year and more ago, and that eight of these, *i.e.*, 61 per cent., are alive and well. These percentages I have placed at the very lowest estimate, because there were four cases about which there was no information obtainable, and, for the purposes of these percentages, I have treated them as persons who died of sleeping sickness. And there is another, No. 14, in regard to which it is stated that the cerebro-spinal fluid and the blood were all right, and that there was only one gland negative; and I understand from this statement that there were some glands that were positive.

Dr. MARSHALL: One palpable gland, but it was negative; no other glands were enlarged.

The PRESIDENT: That being so, instead of eight being alive and well there were nine alive and well; in other words, 69 per cent. of the cases are alive and well at the present moment. I think that to have treated such a series of patients suffering from trypanosomiasis with the success which these percentages represent is a very great and remarkable achievement. And it is the more remarkable when we remember that hitherto the successes have been comparatively few by the other forms of treatment; and it is pretty well recognised that when a case is treated in the endemic area it is pretty well hopeless.

Now it remains to be seen whether the same results can be obtained with the Rhodesian type. I see no reason why it should not, because I look upon this treatment as being based on a scientific foundation; there is using the serum separately on the cerebro-spinal fluid and on the circulating blood, and there is also the preparation of this serum by letting it stand and allowing the products of the trypanosomes to die and excrete their intracellular and extracellular enzymes, or whatever you

may choose to call them. In treating the cerebro-spinal fluid and the circulating blood as different systems the authors are absolutely correct; they are correct in so far that no metallic medicament injected into the blood-stream reaches the cerebro-spinal system. Professor HALLIBURTON, whom we are glad to see here to-night, in his presidential address to the Neurological Section of the Royal Society of Medicine, in October, 1916, treated upon this subject, and showed that this was the case in normal individuals. Perhaps we may have the advantage of hearing him explain this. I am in favour of the trypanolysin theory, because, after all, the treatment which has been advocated just now is very similar in method to that which is used for the curative and preventive treatment by vaccines and antitoxins. It does not matter whether you are dealing with the vegetable world, such as bacteria, or with the animal world, as you are in the case of trypanosomiasis, the enzymes, or the antitoxins, whatever they are, appear to have practically the same action—they have an activating effect on the cells and tissues of the body and render them capable of destroying the parasites. This autoserum therapy is very interesting, and is receiving attention of late. Recently, in the *Indian Medical Gazette*, there is an article by Dr. SENN, of Bombay—an article under the supervision of one of the medical men of the Indian Medical Service— in which some very instructive cases are given of treatment by this serum therapy. In the case of patients who are suffering from certain illnesses, he draws the blood and dilutes it with distilled water, in order that the ferments shall get into the surrounding fluid, and then he injects into the patient this fluid, and some of the results reported are very remarkable.

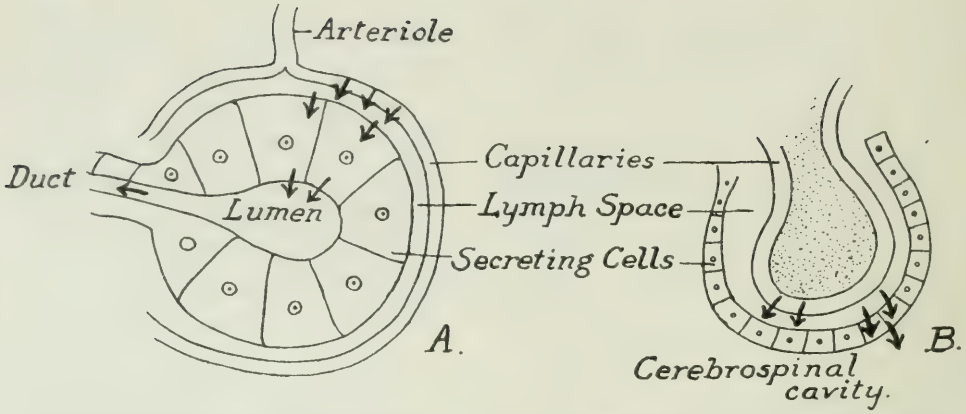
You will have gathered from what I have said that I am very much impressed with the value of this new treatment, and I do hope that some movement will be inaugurated for putting it to the test, not on a small scale but on a large scale. And I agree with Dr. MARSHALL that the veterinarian should come in and assist. But I also think that other scientific men should assist. And I would like to see some of the wealthy men coming forward and helping financially with it. I would like to see a Rockefeller assisting. We want some British Rockefeller very badly to encourage the application of scientific discoveries to our tropical possessions.

You may think I am taking a very rosy view of the researches of

Drs. MARSHALL and VASSALLO, but it is now over twenty-five years since HAFFKINE and myself worked out successfully on men and women the problem of anticholera inoculation, and we began with a much less promising prospect than in the present case. You know that anticholera inoculation has been the foundation of many of the present-day vaccines.

I am sure this paper will give rise to a very interesting discussion, and I hope you will speak freely and criticise the paper, because it is by criticism that people learn. We would like first to hear Professor HALLIBURTON on the cerebro-spinal system.

Professor W. D. HALLIBURTON, F.R.S.: The particular point I drew attention to in the presidential address you have alluded to, before the Neurological Section of the Royal Society of Medicine, the part which bears upon what we are dealing with to-night, is with regard to the normal formation of the cerebro-spinal fluid and its normal function. The cerebro-spinal fluid is a secretion; it is not a leakage fluid, like lymph is from the ordinary blood-stream. If we may compare a salivary gland to the particular mechanism which forms this fluid, I can represent the difference between them in a very simple way on the blackboard. In the salivary gland there are groups of cells, arranged in acini, and each acinus consists of a number of large cells which border the space called the lumen, whence the saliva passes through the salivary ducts. Each of these acini is surrounded by blood-vessels. The blood leaks, and we get lymph formed. Saliva has a composition of its own, and it is of fairly constant composition. So from the blood the exudation takes place to the lymph, and the cells work up the lymph into the new material called saliva, and, ultimately, we get the saliva poured out, at considerable pressure. In the case of the choroid plexus, which Sir FREDERICK MOTT has called the choroid gland, you will find something of the same sort; but in this case the blood-vessels are inside, and they are coated over by cubical cells, which are true secreting cells, and show histological changes similar to those which can be detected in various stages of secretion in the salivary gland. The blood leaks, and gives rise to lymph; these cells take up from the lymph the materials which they want. The direction again is from blood to lymph, then into the cells, which then pour their secretion into the cerebro-spinal space. Just as the saliva is of fairly constant composition, so the fluid which is formed here (see diagram),



and enters the cerebral ventricles and the other spaces, is of constant composition. It is especially important that it should be constant, because that fluid ultimately penetrates to the spaces which surround the nerve cells in the central nervous system. These cells are very sensitive, so that any error in composition of that fluid would produce serious effects on the nerve cells. The cerebro-spinal fluid is sometimes called the lymph of the brain. That is a very slipshod expression. It is contained in channels which resemble lymph channels, but in the case of the lymph there is always the possibility of the passage of the fluid and other materials in both directions, from the blood to the lymph, and from the lymph to the blood. But in the case of cerebro-spinal fluid there is a passage in one direction only; this ideal saline fluid maintains the normal osmotic pressure necessary for the life of the nerve cells; the cells which secrete the fluid take good care that nothing unusual comes through. They form what we may call a barrier to prevent harmful materials from passing into the cerebro-spinal fluid. It is quite true that materials introduced into the cerebro-spinal fluid can get into the blood-stream, but, except for the choroid secretion itself, there is no passage (on account of the guarding action of these choroidal cells) of poisonous materials like arsenic or antimony from the blood. In disease these choroidal cells still maintain their rôle of a stalwart barrier, and foreign materials circulating in the blood are kept back, only the normal fluid coming through. There are one or two very volatile materials which get through, and of these alcohol is one; it is the only one about which we are quite certain. Nature lets alcohol through; hence harmful effects on the nerve cells are produced with comparative

ease by this poison, but metallic poisons are kept back, even in disease. When, in syphilis, spirochætes (or, in sleeping-sickness, trypanosomes) get in by a back door, they have reached a harbour of refuge, they are extra-vascular, and the only way to attack them is, not to inject anything into the blood-stream, because it will not get into the cerebro-spinal fluid, but inject it straight into the cerebro-spinal fluid. That has been tried in the later manifestations of syphilis, such as locomotor ataxy, but the result is similar to that which Dr. MARSHALL has recorded this evening; you not only by this means kill the parasite in its lair, but you also kill the host which harbours it, and the treatment is a good deal worse than the disease itself. Therefore we must be extremely thankful to Dr. MARSHALL and his colleague for finding material which is fatal to the parasite but which is not fatal to the man who harbours it. I think, therefore, that in the explanation which they have advanced on page 12, they have slipped into a misapprehension of what is really the case. They suggest that the action of the trypanosome in the central nervous system is to cause such thickening of the membranes that the connection between the blood-stream and the cerebro-spinal fluid through the choroid plexus is occluded quite early in the disease, and that, as a result, drugs circulating into the blood-stream are not eliminated into the spinal fluid. What occurs in the disease is really on all fours with what occurs in health. The choroidal cells are still healthy, for if they were diseased, they could not maintain their usual office of stalwart guardians and prevent any foreign material passing into the cerebro-spinal fluid. I have very great respect for the encyclopædic knowledge of Sir ARTHUR KEITH, but I think he has gone wrong in what he is quoted to have said in a later part of the same paragraph. It is true that the exact anatomy of the route is unknown; but, he goes on, "there is no doubt that infections in the basal cisterns do reach the cervical glands, and that very probably this occurs through the nerve sheaths." That statement is founded on the writings of a number of French observers a good many years ago. But within recent years my friend, Professor DIXON, and myself, have reinvestigated the matter, and we found that materials introduced artificially into the cerebro-spinal canal did not leave by lymph channels. If you inject material which you could easily recognise, such as methylene blue, no trace of blue passes into the lymph stream; the lymph collected from the thoracic duct

contains none; the blue lines which one would see along the nerves if the lymphatics were filled with blue fluid, are invisible. What does occur is, that the fluid which is being continually formed does not find an exit by the nerves or their lymphatics, but through the microscopic arachnoid villi which project into the venous sinuses mainly at the base of the brain. Within a few seconds after the injection of such a material as methylene blue in the cerebro-spinal canal, although you can find no trace of it in the lymph, you can find it in the blood, and, in a few minutes, in the urine. Communication is not via the lymph-stream, but via the blood-stream, and the arachnoid villi—which WEED and his colleagues in America have described—are now regarded as proved to be the sites of the leakage of the excess of cerebro-spinal fluid back into the blood-stream, but not into the lymphatic system.

Dr. P. MANSON-BAHR: In medical practice in London we have not, of course, access to as many cases of trypanosomiasis, as Dr. MARSHALL has had in Uganda. Nevertheless, from the few cases I have had to treat I have been able to draw some conclusions. The first question, as bearing upon the points under discussion to-night, which I would like to ask is this: Are we quite certain that the invasion of the cerebro-spinal fluid by trypanosomes is necessary in order to produce the sleeping-sickness state? I maintain we are not. I have one case in my wards at present who was infected originally on the Congo in 1916; he had an acute attack of trypanosome fever, typical lymphatic glandular enlargement, with a typical rash, but trypanosomes have been found on one occasion only—in 1919, three years after the onset of the disease. The cerebro-spinal fluid has been repeatedly examined and his blood injected into animals consistently with a negative result. Yet that man to-day, five years after his original infection, presents a typical clinical picture of the sleeping-sickness state. He lies prostrate in bed, with incontinence of both urine and fæces, and a mental degeneration of a severe degree. We have, therefore, no right to say that the sleeping sickness state is invariably caused by a trypanosome infection of the cerebro-spinal fluid!

Another case is one of an officer, also from the Congo, infected early in 1919, who has been under my care for a year. Everything possible in his case has been tried, including Dr. MARSHALL'S treatment. Intravenous injection of salvarsan in doses of 0·6 to 0·8 grammes has

made no difference in the numbers of trypanosomes circulating in his blood. Therefore, in view of this, and in view of experiments upon laboratory animals, I cannot see that there is any justification for assuming that this drug possesses any trypanolytic action, and therefore I cannot understand the contention that salvarsanized serum in trypanosomiasis can have any action whatsoever. Another point to be taken into consideration is the habit which trypanosomes, in this case of *gambiense* type, have of appearing in the blood-stream in a periodic manner. In this case, in spite of atoxyl, antimony tartrate, salvarsan, and other drugs, the trypanosomes appear with regularity about every three weeks; they have been very numerous indeed, numbering as many as 30 to every 200 leucocytes. In this case too, the cerebro-spinal fluid is free from trypanosomes. I carried out the injection of salvarsanized serum, but, beyond making the patient very ill and giving him an intense headache for a week, it had no effect whatsoever upon the circulating trypanosomes.

Therefore, whilst congratulating Dr. MARSHALL on the splendid results of the treatment in his hands, we must look upon this problem in the true scientific spirit and confess that at present there is no specific treatment for trypanosomiasis. I have not had any good results by employing the same methods, nor can I see how the injection of such a small amount of practically normal human serum can have on such a resistant organism!

In any case, I should like to ask him how I have gone wrong in my technique and, in doing so, I would express my very real anxiety for the two cases at present under my care.

In estimating the exact value of the undoubted recoveries from trypanosomiasis (*T. gambiense*)—and Sir PATRICK MANSON and others record some sixteen—we must remember that, as in the case of other protozoal infections, malaria, for example, there is no reason why trypanosomiasis should not be a self-limited disease. Why is it that the malaria parasite (*Laverania malariæ*) kills some people in twenty-four hours and in others produces no symptoms at all?

Several of Sir PATRICK'S trypanosome cases were cured before the days of intravenous medication; they were cured by intramuscular atoxyl and even liquor arsenicalis by the mouth, yet we are not at present blazoning forth either of these two drugs as wonderful

discoveries, specific for the trypanosome, or as opening up a new future for Central Africa, which has actually been stated to-night.

Dr. G. C. Low: The subject of the treatment of trypanosomiasis is a difficult one, and I do not wish, by any criticisms I make now, in any way to damp the enthusiasm of the younger generation in trying to devise better lines of therapy for this serious malady. I think I am specially competent to speak upon this subject, as I began my studies upon it as long ago as 1902 in Uganda, with the first Sleeping Sickness Commission. I saw and studied many cases there, and since that date have had the opportunity of seeing all of Sir Patrick Manson's and Dr. Daniel's cases treated here in England, while, in addition, I have had a considerable series of my own. As one gets older one becomes more dubious as to how far one can definitely say any given protozoal disease is really cured. Take syphilis, for example, a disease due to a treponema, and, although not a protozoal one, akin in many ways to trypanosome infections. When salvarsan was produced, one dose was said to cure anyone, but now we know that even ten doses, plus mercurial treatment as well, fail, in many instances, to bring about the desired result. I would like to ask Professor Halliburton one question: I had an idea that potassium iodide could reach the cerebro-spinal fluid when given by the mouth. Is that so?

Professor Halliburton: Some people say so; I have tried it but failed.

Dr. Low: Well, then, let us admit that it is difficult or impossible for some drugs to reach the cerebro-spinal fluid, and so to reach the trypanosomes, if they lie up there. What proof, however, have we that that is the only place the trypanosomes are resting in? How do we know they do not lie up in the spleen, bone-marrow, or other tissues of the body? If that is so, we have to return to the idea that some of the parasites become resistant against the drugs used, an analogy present in malaria and other protozoal diseases. There are some strains of malaria that are very resistant to quinine, just in the same way as certain strains of the Leishman-Donovan parasite resist antimony. I have a patient now with a leishmanial sore on his nose which has resisted 34 grs. of antimony intravenously, plus full courses of X-ray treatment as well. Even with all

this, parasites can still be cultivated from the lesion. Dr. MANSON-BAHR has told you of similar resistant trypanosomiasis cases to-night, and yet one of these had had Dr. MARSHALL'S exact treatment. One of these cases I saw (for Dr. DANIELS) when the patient first arrived in England, some years ago, and yet, though only a Nigerian case—the type more easily cured than any other—and though having all the different recognised treatments, he is now dying of typical sleeping sickness. I have another similar case under my own care now. Then, again, take the Rhodesian cases; all who have come home to England have died with the exception of one, and he had to have somewhere about 270 grs. of antimony to effect a cure, if he really is cured. Another of these cases lived over two years. He was kept under constant observation during the whole time, and, though in the middle of his time he appeared quite cured and healthy, he finally died, and at the autopsy the typical lesions of sleeping sickness were found. STEVENSON has recently shown that the trypanosome is not so much a blood parasite as was at one time thought; it can escape from the vessels and be found in the general tissues of the brain and other parts. How, then, if it is lying quiescent in the brain tissue, can injections into the spinal canal reach it? The perivascular small-celled infiltration, though well seen round the brain capillaries, is not limited to these areas, but occurs around the small vessels of the heart and generally throughout the body. It is, without doubt, produced by the irritation of the toxins given off by the parasites generally distributed throughout the body.

With regard to Dr. MARSHALL'S table, one must not forget that cases of trypanosomiasis may remain latent for long periods of time. I remember such a case before going to Uganda, that of a boy who died of sleeping sickness in Wales years after leaving the endemic tropical area. Bearing in mind such cases, one must not jump to the conclusion that all Dr. MARSHALL'S patients, even though some of them have apparently been well for thirteen months, are cured. It is rash to conclude that anyone is really cured under three, or one might be safer in saying five years. Some of the old 1902-1903 cases are, or were recently, alive, and one can of course definitely speak of them as having recovered. When I was in Uganda, the epidemic was at its height, and patients were dying in three or four months' time as an average, but even so, some were of a chronic type and lived a year or longer. It is almost

certain, as far as Uganda is concerned, that the disease must have lost this extreme virulence at the present day, and this may easily explain the mildness of Dr. MARSHALL'S cases.

As regards the statement that the meninges are greatly thickened, this is not so. I have done a very large number of autopsies on such cases, and the great majority show nothing macroscopically at all, apart from a slight ground-glass-like appearance of the cortex of the brain. Further, sections confirm this, the small celled infiltration under the meninges being only found in a very thin layer. When the meninges were grossly thickened, secondary infections with organisms were always found.

Let us pass now to the case of the trypanolysin or trypanolytic antibody. Though not denying that some such substance may exist, it does not appear that it can have much potency. I have never heard of any case of natural cure in a white person. Such cases invariably end fatally at varying periods after infection. If the antibody is so potent that the amount contained in twenty drops of serum injected into the spinal-canal can completely sterilise the patient of his whole infection, why cannot it do so when circulating in the blood? Dr. MARSHALL may reply, the antibody cannot get into the cerebro-spinal fluid; but how can he prove this? And besides, as I have already shown, the idea that the trypanosomes are only present in the cerebro-spinal fluid in sleeping sickness is begging the question.

I do not know if Dr. MARSHALL is aware that an exactly similar theory was put forward for para-syphilitic conditions, such as general paralysis of the insane and locomotor ataxia, the idea similarly being that the treponema was locked up in the nervous tissues and that drugs given by the blood could not reach them. For this, salvarsanized serum was injected into the spinal canal, and even into the lateral ventricles, with, I believe I am correct in stating, absolutely negative results. If so, then I personally cannot see how a similar treatment will succeed in trypanosomiasis when it has failed in syphilis.

One does not like, as I have already said, to damp enthusiasm or to throw cold water on any new work. No one would be more pleased than myself to know that we had at last a definite cure for trypanosomiasis and its late sequel, sleeping sickness; but in this case I must say distinctly that the verdict is "not proven." Till we have further work accurately

and scientifically carried out, it is premature to talk of this treatment as a cure, and it is not fair, by making such statements, to build up the hopes of those unfortunate individuals who happen to be suffering from the disease.

I honestly cannot see how injecting a few doses of the patient's own serum into his cerebro-spinal fluid is going to cure him. Nor can I believe that one injection of salvarsan will cure any case of trypanosomiasis. (*Vide* remarks on syphilis.)

Take the case even of the gentleman who has attended to-night. Six weeks after the treatment, trypanosomes were found in his blood, and since that inoculated animals have become infected. How can one talk then of this man being cured, even though no trypanosomes are present at the moment, especially after having heard from Dr. MANSON-BAHR of his case, where, though no trypanosomes have been found for a long time in the cerebro-spinal fluid nor in inoculated animals, yet the man is dying of sleeping sickness.

Lieut.-Col. R. H. ELLIOT: May I intervene in order to give a new turn to the discussion? A number of us are very greatly interested in Dr. MARSHALL'S work, and we feel that that work ought to be given an opportunity for further continuation. We, therefore, think that whether he is right or wrong—and many of us do not feel competent to discuss that subject on the higher planes—this plan of treatment should be given a very full trial. I would further suggest that, if possible, some report should be made to the Colonial Office by this meeting, with a view to facilities being afforded for the investigation of the method of treatment now advocated, not merely from the point of view of human trypanosomiasis, but also from that of animal trypanosomiasis. We, many of us, know the tremendous amount of thought and anxiety which trypanosomiasis is giving to the Government of Uganda at the present time. I am in frequent touch with one who is engaged on work in connection with sleeping sickness, and I, therefore, feel a very personal interest in the subject. If this new line of treatment is right, there are enormous advantages to be gained from it, and the commission of investigation should not work at a disadvantage. The disadvantages of trying the new method of treatment, even if it prove useless, are negligible, but the advantages, if it is right, are very great. I am in a position to say that

some of us have reason to believe that if any such movement is put on foot, we should not find it very difficult to put our hand on a good deal of money for the purpose.

Dr. E. T. JENSEN : Colonel ELLIOT said money would be forthcoming for this. I think I am within the facts when I say a substantial sum has been promised if this scheme is approved by the tropical diseases section of the medical profession. Will you ask, sir, whether this meeting approves of Dr. MARSHALL'S treatment being tried out ?

Lieut.-Col. ELLIOT : I second that proposal, that every facility be given for Dr. MARSHALL'S work to be carried further, with a view to it being thoroughly tested.

This was put to the meeting and carried *nem. con.**

Sir HUGH CLIFFORD said that even if only a small number of cures could be effected by Dr. MARSHALL'S method, experiments to test it should be systematically carried out. There were many Medical Officers on the West African Medical Staff competent to take charge of such researches, and he would urge the Colonial Office that such experiments should be made in Nigeria, for which his Government would not grudge a few thousand pounds.

Dr. W. T. PROUT : I shall not say much about the technical part of this paper, except that I do not take quite such a pessimistic view of the matter as do Dr. LOW and Dr. MANSON-BAHR. I do not think Dr. MARSHALL has gone so far as to make a definite claim that this is a cure ; he has simply said the indications, so far, are very hopeful ; that this is a method which has afforded relief in a considerable number of cases for a considerable period ; and, I think, we may hope that this new line which is being carried out will prove fruitful. I think the facts which have been put forward are sufficient to justify us in encouraging him in every way to carry out further investigations. So far as the patient who is here to-night is concerned, I have seen him since he returned to this country in December last, and his improvement has been progressive. It will be agreed that to-night he looks even aggressively healthy, and the last report of Professor EYRE was that he

* This resolution was *ultra vires* as previous notice had not been given.

did a lumbar puncture and there was no increase of pressure; he inoculated two mice and one rat, and they were unaffected, the cerebro-spinal fluid has been centrifuged, and the blood examined carefully, and it has been found negative. There has been no repetition of these periodic outbursts while he has been in this country, and there are very strong grounds for believing he has got rid of these parasites. I do not think the analogy with malaria which has been made is quite a fair one. We know it is self-limiting in a few cases, that persons lose the disease without treatment; improved conditions of life enable them to get rid of the parasite. I do not know of any case in which trypanosomes have been swarming in the blood and the disease has proved to be self-limiting.

With regard to the question of a further investigation, I shall have an opportunity of putting the matter before the Colonial Office, and shall support the scheme in every possible way.

Dr. MANSON-BAHR: May I say a few words in explanation of Dr. PROUT'S dictum upon the pessimism of the physicians of the Hospital for Tropical Diseases, of which I am one. No one, I would assure him, would hail with greater pleasure than Dr. Low and myself the discovery of a real cure for trypanosomiasis. At any rate, I can assure him that we will continue to follow this work with very great interest, but he must remember that we have been following up the few cases for over two years, not for a period of a few months.

Dr. C. F. HARFORD: I do not wish to enter into the technical aspect of this question. It is 31 years since, in Nigeria, I knew of sleeping sickness, and my interest in it has been maintained ever since. I think there is a difference in the cases treated in the country in which the disease has arisen and those which have filtered through into this country and are treated here; they cannot, I think, be put into the same category. In the trypanosomiasis-infected countries there are far greater opportunities of having light thrown on the matter than here, and that may be one cause of the difference in the results of observation.

I hope this matter will be taken up by the Colonial Office; I am sure it must have struck all of us who have heard this remarkably interesting story that it is a matter which should be probed to the bottom.

The PRESIDENT: I think there has been some misapprehension in regard to treatment. Dr. MANSON-BAHR has spoken about kharsivan, antimony and other drugs, and so has Dr. LOW. The kharsivan is only an activator of the ferments which are in the body. The injection of drugs into the circulation or into the spinal cord is not the only or even the chief basis as I understand of this new treatment of trypanosomiasis. It is only a part. The treatment is to make use of the trypanolytic properties of a serum which has in a high degree acquired those properties by several combined processes, such as the natural increase of power of enzymes or antibodies secreted in the blood and tissues when the body is invaded, the further increase of enzymes or antitoxins on the multiplication and death of trypanosomes in the blood while in the body, and the still further addition of enzymes to the serum on the death of the trypanosomes after the blood containing them has been withdrawn from the body and kept in a vessel.

Dr. MARSHALL: After so much has been said in the discussion, it is difficult for me to take up the points which have been raised.

I am grateful to Professor HALLIBURTON for the way in which he has cleared up the point in regard to the choroid plexus—one which we did not understand before.

Dr. MANSON-BAHR and Dr. LOW quote cases of malaria and syphilis as good parallels. In some cases quinine and salvarsan respectively have no effect on these diseases; but surely that is no reason why quinine and salvarsan should not be tried in ordinary routine cases. Dr. LOW spoke of the results in natives. The European has a higher resistance to the trypanosome than has the native, and if one has cases of natives going two years without treatment and remaining well, it is a sign that at any rate they have improved, even if they have not been cured. With regard to Mr. Rubie, and the possibility of his not having been cured, he does not look very ill at the present moment.

I am very grateful to his Excellency, Sir HUGH CLIFFORD, for what he said in regard to administrative support, and on behalf of Dr. VASSALLO and myself, I wish to say we shall welcome any further tests in order to carry these results to absolute completion, so as to decide, one way or the other, whether or not there is anything in the treatment

SOME POINTS CONCERNING TRACHOMA.

BY

LIEUT.-COLONEL H. KIRKPATRICK, I.M.S.

It is hardly necessary to lay stress upon the importance of trachoma when addressing medical men who are practising or who are about to practise in the tropics. As you are well aware, the disease is one of the great causes of blindness and loss of efficiency in the Near and Far East.

Trachoma is associated with bad housing conditions, dirt, and general insanitary surroundings. When dust and glare, which lower the resistance of the conjunctiva to infection, are added to these conditions, then a state of affairs highly favourable to the spread of the disease is produced. The zenanas of the poorer class Mohammedans form never-failing reservoirs of infection from which the disease can spread, first to other members of the family, and then to those outside the family circle. The henna pot, which contains a pigment for beautifying the eyes, and which is shared, in a communistic fashion, by the ladies and children of the family, is a fruitful source of infection.

Flies may occasionally be responsible for the spread of the disease, but many authorities now consider them to be an unimportant factor in the dissemination of infection.

Trachoma is common in the Eastern parts of Europe where insanitary conditions prevail, but, fortunately, it is now rare in England, though this country, in common with other parts of Western Europe, was flooded by a wave of infection in the beginning of last century on the return of the soldiers who fought in the Napoleonic wars. The backwash of this wave is yet apparent in Ireland, the less progressive districts of which country are still infected. In England the disease is now chiefly seen amongst immigrants from Eastern Europe.

Trachoma ($\tau\rho\alpha\chi\upsilon\varsigma$ = rough) is a specific and infectious inflammation of the conjunctiva, of a chronic type, and is characterised by the

formation in the membrane of follicles and papillæ which end in cicatrisation. The disease is frequently called granular ophthalmia, an unfortunate term, since it lays emphasis upon the occurrence of follicles and papillæ which are merely the reaction of the conjunctiva to any form of chronic irritation, and are in no way pathognomonic of trachoma.

Before proceeding further, I propose to recall to your memory certain facts concerning the structure of the conjunctiva. The conjunctival membrane, which has a close relationship to the skin, is continuous with the skin at the margins of the lids. It sweeps backwards over the tarsal plates, to which it is intimately attached, and, forming a very lax fold, or fornix, above the convex border of the tarsus, passes on to the anterior surface of the globe and gives a loose covering to the front portion of the scleral tunic. The conjunctiva is represented on the surface of the cornea by the corneal epithelium.

There are thus three separate parts of the conjunctival membrane: (1) The tarsal or palpebral; (2) the fornical or transitional; (3) the bulbar. The tarsal and fornical parts of the conjunctiva are covered by laminated cylindrical epithelium and there is a considerable development of low papillæ in the former. As these papillæ are covered by epithelium, they do not become evident on the surface until inflammation causes them to hypertrophy. At the junction of the tarsal and fornical portions of the conjunctiva these papillæ become higher and the epithelium dips between them, so that the discrete structures may give a velvety appearance to the membrane. This appearance is very marked in the presence of inflammation, but it may also be found in some cases of simple hyperæmia caused by an error of refraction. A delicate reticulum of adenoid tissue appears in the deeper layer of the conjunctiva at an early age, and is best marked in the transitional portion of the membrane. This tissue may show follicular aggregations even in the healthy membrane, but such formations are much more evident if any chronic source of irritation is present.

Pathology of trachoma.—A section of a trachomatous conjunctiva shows a general round-cell infiltration of its deeper layer with a varying degree of vascular engorgement. Pseudo-papillæ, formed by folding of the swollen membrane, are found, especially in the transitional part of the conjunctiva; tubular depressions, lined by epithelium, are also seen, and cysts may be caused by the occlusion of their orifices or of the

mouths of the interpapillary crevices and by the subsequent accumulation of epithelial debris. The epithelium is thickened and is infiltrated by leucocytes, and actual downgrowths of epithelial cells may occur into follicles which have ruptured.

The follicle is the characteristic and striking histological feature of trachoma; it is composed of a central group of large connective tissue cells having rounded or oval, pale nuclei, and of a peripheral group of small and deeply staining lymphocytes; the centre of the follicle appears to be paler than the periphery for this reason. The central cells may be mononuclear leucocytes, or may be connective tissue cells, and often appear to be epithelioid, and their cytoplasm may contain cell inclusions of various kinds. Other forms of leucocytes may also be found in this zone. The peripheral cells are enclosed in a stroma which is continuous with the connective tissue of the surrounding conjunctiva, but it is a disputed point as to how far this stroma extends into the interior of the follicle. The follicles are surrounded by a vascular network from which capillaries pass inwards, but these do not appear to reach the centre of the follicle. The existence of a capsule, in the early stages of the follicle, has been disputed, but a capsule undoubtedly forms in the later stages and takes its part in bringing about cicatrisation. It has been stated that the capsule begins to form on the deeper surface of the follicle, and that it is best developed in that part. The follicle ends in cicatrisation, which is generally preceded by a degeneration and softening of its contents. The softened contents may, occasionally, be discharged on the surface, the covering epithelium having become thinned and broken through; but an ingrowth of fibrous tissue, followed by absorption, is the more common termination.

Infiltration of the tarsus by round cells, which is best seen along the course of the vessels, is found at an early stage, and this is followed by distortion and, in some cases, by a partial atrophy of the tarsal plate. The tarsal glands undergo degenerative changes, and the formation of cystic spaces in them is fairly common.

Pannus is seen as a cellular infiltration of the superficial layers of the cornea, accompanied by a rich formation of young blood-vessels. The infiltration, in the early stages, is usually quite superficial and lies between the epithelium and Bowman's membrane, but in the later stages the *substantia propria* is involved, and Bowman's membrane may

be destroyed in advanced cases. Nodular aggregations of lymphocytes may be found which resemble the young follicles seen in the conjunctiva, but typical follicles rarely occur except upon the limbus.

No specific organism has yet been discovered to be the cause of trachoma. PROWAZEK and HALBERSTAEDTER have described groups of corpuscles in the epithelial cells which they considered might be the cause of the disease. Similar appearances have, however, been found in other conditions, and even in the apparently normal conjunctiva. HEYMAN has found identical forms in cases of blenorrhœa, and GREEF states that "the conclusion that everything, in which trachoma bodies can be found, is trachoma, can no longer be sustained."

Symptoms and Signs of Trachoma.—The disease may be divided into three stages:—(1) An early or florid stage, which is chiefly characterised by the formation of follicles and papillæ; (2) a middle or early cicatricial stage, in which traces of fibrous tissue can be distinguished by the unaided eye as it forms in and amongst the trachoma follicles; (3) a late stage, in which the tarsus and cornea show marked changes, due to the disease, and in which the cicatricial changes in the conjunctiva are very advanced. It is scarcely necessary to mention that no sharp line can be drawn between these different stages, which gradually merge into one another; the forms of the disease may also be considerably modified by the occurrence of secondary infections.

First Stage.—The appearance of small papillary elevations, accompanied by a few irregularly placed follicles, is usually the earliest sign of trachoma. These signs are often said to make their first appearance in the lower fornix, but, at a very early stage, they are best seen at the convex upper edge of the superior tarsus, and, indeed, this portion of the conjunctiva bears the brunt of the attack during the greater part of the disease. Follicles increase in number and are seen on the tarsal conjunctiva as small, raised, yellowish, and irregularly placed spots. Their growth in this region is limited by the intimate connection that exists between the membrane and the tarsus, but they reach a much greater size in the transitional conjunctiva, where their growth is less restrained, and here they are of varying sizes and are pale and translucent, resembling sago grains or frog-spawn. Considerable swelling of the transitional conjunctiva accompanies the formation of the follicles, and small folds and creases of this part of the membrane are formed and lead

to the appearance of coarse papillæ. The papillæ, which normally exist in the tarsal conjunctiva, undergo hypertrophy as a result of the irritation, and, by doing so, often hide the follicles. The proportion of follicles to papillæ varies in different cases and sometimes one predominates and sometimes the other, so that a "papillary" form and a "follicular" form of trachoma have been described; it must be remembered, however, that the follicle is the essential feature of this stage, and that, though it may not be immediately apparent, it is never absent. The occurrence of a secondary infection will favour a papillary outgrowth and so cause a papillary type of the disease.

It is necessary to evert the fornix thoroughly in order to examine the transitional conjunctiva properly; this may be effected by many different means, of which eversion of the lid by a small button-hook is very effective, but *by far the most satisfactory method is to balloon the conjunctiva by injecting a syringeful of normal saline beneath it*; any changes in the membrane can then be accurately observed as it lies stretched and fully exposed. This method has the further advantage, as will be pointed out later, that it allows remedies to be thoroughly applied to the diseased area and is otherwise beneficial. The occurrence of follicles in the fornix is usually limited by a fairly regular line that lies just anterior to the junction between the transitional and the bulbar conjunctiva.

Ptosis can be nearly always observed at this period, even in the early stages; this drooping of the lid is most probably due to a loss of function of the levator palpebræ owing to its insertion having become involved in the inflammation. *Pannus*, or vascularisation of the cornea accompanied by some opacity, due to subepithelial infiltration, may or may not be present in this stage, but, if the cornea is carefully examined, it will usually be possible to detect a slight swelling of the upper part of the limbus associated with the presence of some fine vascular twigs, which branch on to the neighbouring corneal tissue.

Middle Stage.—All the signs become more accentuated in the middle stage of the disease. Ptosis is obvious and pannus becomes more marked, and often involves the whole of the upper half of the cornea. If the transitional conjunctiva is ballooned by an injection, delicate lines of fibrous tissue can be seen running through it, so that it appears as if a fine grey net had been pressed into the membrane and had been

incorporated with it. A line of fibrous tissue may also be observed to run horizontally about 3 mm. above the free edge of the lid in the *sulcus subtarsalis*, at the point where the *rami perforantes* pass from the inferior tarsal arch of vessels to the conjunctiva through the tarsal plate. This line becomes broader and deeper, and is known as *Arlt's line*. The internal margin of the lid, which normally has a sharp and well-defined edge, becomes rounded, and a soft granulation tissue often forms upon it. When the follicle formation is in excess, the follicles on the tarsus sometimes become aggregated into an almost homogeneous, firm, gelatinous mass, which is of pale yellow colour ; a considerable thickening of the lid may be produced in this way ; the surface epithelium becomes thickened at the same time, and the whole syndrome forms the condition which is known as *Stellwag's gelatinous trachoma*. Cysts may also form in the conjunctiva as the result of the retention of cell products in the crevices between the papillæ and of the accumulation of glandular secretion. Signs of the previous existence of trachoma can often be observed, even if the disease has been cured in the early part of its middle stage. The tarsal conjunctiva will, in that case, be seen to have a faint lilac tinge, which is quite characteristic, and some contraction of the fornix will usually be apparent. In the later part of the middle stage the shrinking of the fornix is much more striking, and it may be possible to recognise definite strands of fibrous tissue in the conjunctiva.

Third Stage.—The changes in the third stage are due to shrinking of the new-formed fibrous tissue and to degenerative changes in the tarsal plate. The tarsus becomes rather sharply bent, so that an angle, whose apex looks forwards, is formed in the lower part of the plate. The tarsus is also reduced in size, and may, in some cases, be merely represented by a small rod-shaped mass of tissue, which contains fat, cheesy matter, and fibrous tissue. These alterations are due both to the degeneration of the tarsal plate and to the traction of the shrinking conjunctiva upon its deep surface. The bending of the tarsus leads to an entropion, so that the lashes turn inwards, and a trichiasis, or rubbing of the cilia on the cornea, adds to the corneal irritation and pannus. Shrinking of the conjunctiva leads to a diminution in size of the transitional fold, and much of the anterior layer of this fold is drawn down to form a covering for the upper part of the tarsal area of the lid. The conjunctival surface of the tarsus shows white branching strands of scar

tissue, and between these strands may be seen small spots of granulating tissue which represent the remains of hypertrophied papillæ. The lid margin has a sinuous outline, described by HERBERT, the portion near the outer canthus being at a lower level than the central and inner parts. The size of the palpebral aperture is also often lessened. Pannus is very marked in this stage and corneal ulceration may occur; the corneal troubles are much aggravated by any trichiasis which may be present. In very severe cases, where the cicatricial changes and shrinking of the fornix have led to an excessive atrophy of the conjunctiva, changes occur in the surface epithelium, the uppermost layer of cells undergoing keratosis with a general deposition of keratohyalin, so that the membrane becomes epidermoid in character. Under such circumstances the eye becomes dry and no tears adhere to the surface of the diseased conjunctiva. This condition of *xerophthalmia* is not limited to the conjunctiva, but affects the surface of the cornea, and, by causing its opacity, leads to blindness.

Diagnosis of Trachoma.—It must be admitted that the diagnosis of trachoma, before the cicatricial stages have set in, is a problem of considerable difficulty, and even a surgeon of considerable experience will frequently find himself unable to decide whether a conjunctival disease is truly trachomatous or not These difficulties are not so pronounced, of course, in the later stages, when cicatricial changes have occurred. The reason is that follicle and papillary formation are the natural reaction of the conjunctival membrane to many different varieties of irritation, infective and otherwise The follicle formation which results from the excessive use of atropine in susceptible persons is an example of one of these, and I have known cases of irritation from this cause to be diagnosed as trachoma. This difficulty of diagnosis must necessarily continue as long as we are unable to identify the causative organism of the disease. Three signs are of value as an aid to diagnosis in the early stages of the disease; these are (1) the presence of ptosis, (2) the early occurrence of pannus in the upper part of the cornea, (3) the situation of the trachoma follicles. Ptosis, of some degree, is seldom or never absent, and the patient acquires a peculiar sleepy appearance owing to the drooping of the upper lid. Pannus appears in that part of the cornea which is in constant contact with the rough and infected membrane, and is first seen at the upper part of the limbus, but the

vascularised area of infiltration soon encroaches upon the upper part of the cornea; this area is generally limited by a fairly well-defined and regular horizontal margin below, which, in the early stages of the disease, does not ordinarily reach lower than the level of the upper border of the undilated pupil. Vascularisation, which commences in parts of the cornea other than its upper half, is unlikely to be due to trachoma.

The follicles, in trachoma, are best marked along the upper, or convex margin, of the superior tarsus, and from here they spread upwards to the fold of the fornix, and downwards on to the conjunctiva which covers the tarsus. They may be seen to a much less extent in the lower fornix and the conjunctiva of the lower lid, and, in some cases, they may even be found upon the plica semilunaris. The follicles are of varying size and are rather irregularly placed, whilst some may be masked by the development of papillæ.

The conditions which are most difficult to distinguish from the earlier stages of trachoma are (1) Follicular conjunctivitis, (2) spring catarrh, (3) a chronic form of purulent ophthalmia.

Follicular conjunctivitis is the disease that presents the greatest difficulty in diagnosis, since it also is characterised by the appearance of follicles, which, however, differ from those of trachoma in that they do not undergo cicatricial changes. Follicular conjunctivitis is not usually accompanied by ptosis, and, unless the conjunctiva is irritated by caustic applications or by secondary infections, shows little tendency to papillary formation or to pannus. The follicles are regular in size and in shape, and are as marked in the conjunctiva of the lower lid as in that of the upper; indeed they may be often rather more so. Follicular conjunctivitis is usually a condition of childhood, and is often associated with an excessive development of adenoid tissue in the naso-pharynx, in the cervical lymphatics, and in other parts of the body. A hyperæmia, induced by an uncorrected error of refraction, or by a mild secondary infection, will sometimes increase the follicular growth and cause the formation of papillæ and so render the diagnosis especially difficult. In cases of difficulty it is advisable to use mild lotions, to correct the refraction, and to watch the course of the case; if the disease shows no signs of progress, it is not true trachoma.

Spring catarrh is characterised by a papillary formation in the conjunctiva of the tarsus and in the transitional conjunctiva. The

Fig. I.

Section under low magnification showing tarsus, tarsal conjunctiva, and transitional conjunctiva in the early part of the second stage of trachoma. Trachomatous follicles and interfollicular depressions are seen in the transitional conjunctiva.

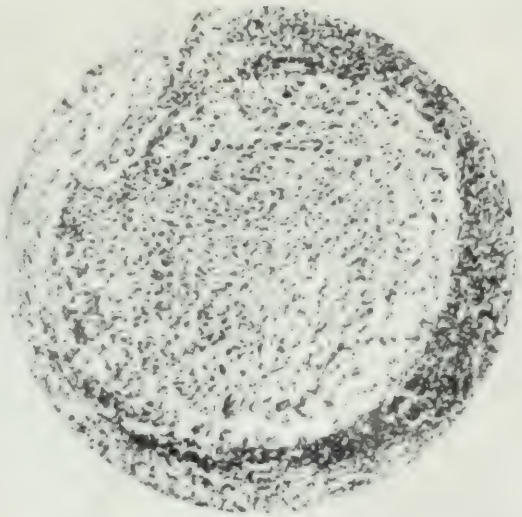


Fig. II.

Trachoma follicle showing peripheral zone of small, deeply-staining cells and central area of large cells. Young blood-vessels seen in periphery, and early capsule formation.

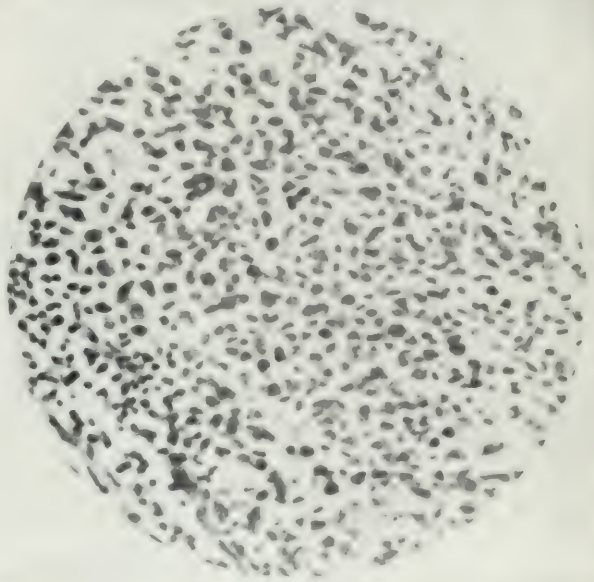


Fig. III

Trachoma follicle, central zone. Note variety of cells.

To accompany Col. Kirkpatrick's Paper (Face p. 42)

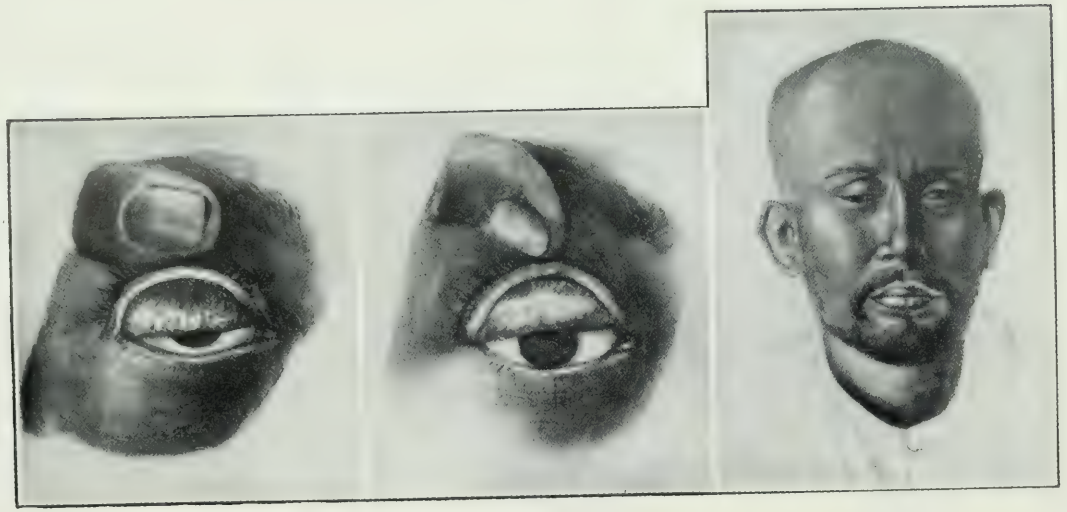


Fig. IV.

Later part of First Stage.

Fig. V.

Later part of Second Stage. Ault's line is well marked. Note the presence of soft granulation tissue on margin of the lid.

Fig. VI.

Third Stage.—Ptosis and the bulging forward of the tarsus seen in right eye. Herbert's sinuous lid margin seen in left eye.

papillæ are discrete and firm, with flattened tops, and, unless inflamed, are pale and pink with a peculiar bluish tinge. The colour is sometimes compared to that of ham. The papillæ are thus quite different in appearance to the softer and readily bleeding papillæ found in trachoma. The conjunctival discharge contains a considerable number of eosinophile leucocytes, and the disease is usually accompanied by an eosinophilia. An absence of follicle formation is a further point of differentiation between the diseases. A spring catarrh, associated with a secondary infection, may present considerable difficulties in diagnosis from trachoma; in such cases a careful examination should be made of the discharge for the presence of eosinophiles. Little difficulty will be experienced in forming a diagnosis if the characteristic corneal changes of spring catarrh are present. Trachoma and spring catarrh are sometimes combined, and such cases will be difficult to diagnose and to treat correctly.

High papillæ, which are soft and bleed readily, and which are accompanied by some irregular follicles, are sometimes found in cases of *purulent ophthalmia*, the acute stage of which has passed off. The papillæ, in cases of this sort, are usually larger than those found in trachoma and a thin, greenish-yellow discharge may be seen to trickle from the spaces between them. An examination of the discharge will show the presence of the causative organism, which is usually the gonococcus. Pannus is absent in these cases, but there may be a vascularisation of the corneal edges, which is not confined to the upper part of the cornea. An inflammation of this character will yield to suitable treatment more readily than trachoma will; the disappearance of the papillæ, after a short course of treatment by eyebaths of magnesium sulphate lotion, aided by the use of copper sulphate, will show the nature of the disease. It should be remembered that trachoma is sometimes complicated by the onset of an attack of gonorrheal ophthalmia; this is said to occur very frequently in Egypt.

The hyperæmia and other conjunctival changes, produced by *an uncorrected error of refraction, is the condition which is most often confused with trachoma by those who are unfamiliar with eye diseases.* Such a refraction error frequently causes a hyperæmia of the conjunctiva and the eyelids, and an increased glandular activity follows the excessive supply of nutriment. This is shown, not only by watering of the eye, but also by the collection of secretion along the edges of the lids, and,

occasionally by the formation of so-called Meibomian cysts or chalazia. The redundant secretion affords a medium in which micro-organisms can grow and multiply, and its presence lowers the resistance of the conjunctiva to infection, so that inflammations of the membrane are common in such cases. Small papillæ and follicles may be found in the transitional conjunctiva, and, as previously stated, if these are irritated by the application of caustic drugs, the hyperæmia is increased and a condition closely resembling true trachoma may be produced. The result of treatment will usually show the nature of the case. Patients who have a seborrhœic tendency and who suffer from an error of refraction, appear to be specially liable to this condition, and the use of resorcin (in 1 per cent. eyedrops), in addition to the correction of the refraction error, is often valuable in such cases.

The Treatment of Trachoma may be considered with reference to the stage of the disease and with reference to whether it should be medicinal or operative.

Treatment should be directed towards promoting the disappearance of the follicles without, at the same time, causing the formation of an excessive amount of fibrous tissue. Nature will, in course of time, effect the first object, but she does so by a cicatrisation that leads to very undesirable complications and sequelæ.

The first essential is that the patient should be placed under good sanitary and hygienic conditions, so that he may be kept in as good a state of general health as possible, and that he may cease to be a source of danger to others. Good food, fresh air, general cleanliness, and suitable tonics fulfil the first requirement. The provision of separate basins and towels for the patient, the observance of proper precautions regarding the cleansing of the eyes by attendants, and the right disposal of cloths soiled by conjunctival discharge, will, under ordinary circumstances, satisfy the second. Should the disease appear amongst members of a community, such as those living in schools or barracks, infected persons should be segregated and placed in special companies or taught in separate classes. The mistake made at the beginning of last century, when infected soldiers were discharged to their homes, and thus allowed to disseminate the disease broadcast, should be avoided, and these patients should not be allowed to return to their families until they are free from infection.

For the treatment of the first stage of the disease, nitrate of silver solution and copper sulphate, or blue-stone, are probably the two drugs which are most in favour as medicinal applications. Silver nitrate is used in various strengths, from 5 grains to the ounce of distilled water to 60 grains to the ounce, but a solution of 10 grains to the ounce will usually be found to be the most satisfactory; the stronger solutions are too irritant and are likely to cause too great a formation of fibrous tissue, whilst the weaker ones are insufficient to cause a proper reaction and to promote absorption. A mop, made by twisting a little cotton-wool on to the end of a small stick (for example a match), is dipped into the solution and then applied to the affected area, the excess being washed off by a stream of saline solution after a pause of about twenty seconds. This may be applied daily or three times in a week according to circumstances. The application is followed by the formation on the surface of the conjunctiva of a bluish-grey film, composed of necrotic epithelium; this is shed in the course of a few hours. Patients occasionally complain that they notice haloes around lights after treatment by silver nitrate; this symptom arises from the effect of the drug upon the corneal epithelium, changes in which cause a dispersion of light. The appearance is only a temporary one, but patients may be alarmed by its occurrence, since a similar symptom is common in glaucoma.

Sulphate of copper should be applied in the form of a stick, or of a crystal which has a perfectly smooth surface. The retrotarsal fold is thoroughly exposed and the crystal, or stick, is lightly rubbed over any prominences which are seen on the surface of the conjunctiva; the conjunctival sac is then thoroughly irrigated with saline solution. The use of copper sulphate is specially indicated in cases where papillary formation is a marked feature. Strong solutions of perchloride of mercury (1 in 100 or 1 in 500) have been recommended by some surgeons; these are rubbed into the affected area with a mop, the pressure of which at the same time forces out the contents of the follicles. Some advocate the application of boracic acid powder in the same manner, and this has the advantage that it causes little irritation. HERBERT recommends intensive irrigation with 1 in 3000 perchloride of mercury solution. Whatever drug be favoured, it is essential to apply it to that part of the conjunctiva which is diseased, and the fornix must be thoroughly everted for this purpose. *A subconjunctival injection of fluid, which balloons out the*

fornix, will be found to be a most efficient method of ensuring a complete exposure of the membrane. The upper lid is everted and the point of the needle is entered at the outer angle of the upper margin of the tarsus, and a syringeful of normal saline solution is injected. If 4 minims of a 4 per cent. solution of cocaine, or similar substance, and 4 minims of adrenalin are added to the saline, any subsequent manipulation of the conjunctiva will be rendered painless. A subconjunctival injection has further great advantages, since (1) it stretches the membrane and so tends to lessen the contraction caused by cicatrisation, and (2) it promotes the absorption of inflammatory products by a lymphagogic action. Puncture of the follicles by a needle or by the point of a galvano-cautery has been recommended by some surgeons of experience, but the expression of their contents is probably the most efficient method of dealing with the follicles at this stage. Expression is carried out by means of a forceps, between the blades of which the diseased membrane is squeezed. The blades of some of such forceps are furnished with rollers in order to facilitate expression of the follicles. A preliminary ballooning of the fornix by the subconjunctival injection of an anæsthetic fluid is advantageous in all these methods of treatment.

The application of carbon-dioxide snow and exposure to X-rays have been recommended in the treatment of trachoma, but these measures have not proved entirely satisfactory in my experience.

It must be borne in mind that trachoma is an obstinate disease, and that, even if detected in the first stage, it will require treatment for some months, if all danger of relapse is to be avoided. If the disease fails to respond to treatment, or if the patient is unable to afford the time necessary for a thorough cure, it may be advisable to undertake a more radical measure and to excise the transitional portion of the conjunctiva.

Such an excision is a simple proceeding; the lid is everted and the fornix ballooned; a slightly curved, horizontal incision is made beneath the follicle-bearing area, and its extremities are then joined by a similar incision passing along the upper margin of the tarsus. These incisions should be quite superficial and should merely divide the conjunctiva. The elliptical area, thus isolated, is then easily lifted from the subjacent tissue by the knife or scissors; the cut edges of the membrane may be slightly undermined and then united by three or four sutures, but this is not really essential, as healing takes place rapidly. This little operation is followed by very little trouble or discomfort.

A trachomatous conjunctiva, owing to its impaired power of resistance, is very subject to the occurrence of secondary infections, and these should be carefully watched for and appropriately treated when recognised. Inflammation due to the Morax-Axenfeld bacillus is one of the most common of such infections, and this will usually readily yield to treatment by sulphate of zinc drops. Koch-Weeks infections are best treated by silver nitrate, and eyebaths of a saturated solution of magnesium sulphate will be found useful in the case of infection by the gonococcus. The latter form of treatment is also of great value in inflammations due to streptococcal infection.

The treatment of the second stage of the disease is conducted on the same lines as that of the first stage, but, owing to the presence of the newly-formed fibrous tissue, medicinal treatment is unlikely to be as effective in this case, and operative measures are more likely to be required. Copper sulphate is usually more efficacious than silver nitrate at this stage, but the course of treatment will probably be much shortened if more radical treatment is adopted. Colonel HENRY SMITH recommends the employment of subconjunctival injections of cyanide of mercury, and ABADIE has recently reported excellent results from deep and multiple punctures of the tissues at the upper margin of the tarsus by a galvano-cautery; the punctures are repeated until a regular trough is formed in the tissues. It will be found, however, that the *combined excision of the fornix and tarsus*, as described by HEISRATH, will probably prove the most satisfactory form of operation. This operation can be very easily carried out if attention is paid to the following steps:—

After ballooning the fornix by the injection of a local anæsthetic combined with adrenalin, a suture is passed through the thickness of the lid at the central point of its margin; this suture serves as a landmark, and assists to control the lid. The upper lid is everted, and the retro-tarsal fold is seized by a fixation forceps and thoroughly exposed; a fixation forceps, provided with a catch, is applied to the outer part of the fold (the inner part in the case of the left eye) and allowed to hang free, in such a manner that full eversion is obtained (Fig. VII). The inner part of the fold (or the outer in the case of the left eye) is next grasped by a forceps held in the left hand, and the tissue is stretched between the two pairs of forceps. A horizontal incision is made through the conjunctiva, just below the follicle-bearing area, along the whole length of the lid

(Fig. VII, 3). A sharp knife is required for this purpose, and care must be exercised to keep the plane of the blade at right angles to the surface of the membrane. The conjunctiva, which forms the lower edge of the wound, is then thrown down towards the globe, so as to form a loose fringe of membrane (Fig. VIII, 5). The fornical conjunctiva is next peeled upwards off the underlying tissues as far as its attachment to the tarsus. This dissection is made more by pushing movements of the blade of the knife than by actual cutting, and it is usually only necessary to divide a few strands of tissue by the knife edge. The extremities of the wound are next joined by a second incision which passes close to the border of the lid (Fig. VII, 4) ; the centre of this incision is deepened until the tissues which underly the tarsus are exposed (Fig. VIII) ; the incision in the tarsus is then completed by seizing the lower margin of the wound, already made, in a forceps, and by extending the cut laterally through the entire thickness of the tarsal plate. The tarsal plate is next dissected off the tissues beneath as far as its upper margin, so that it only remains in position along a narrow horizontal line ; the tarsus and the attached apron of transitional conjunctiva are now held up by a forceps, between the blades of which both structures are grasped, and the remaining attachment is divided by a few strokes of the knife or by a few snips of the scissors. A fairly extensive, elliptical, bare area is left by the removal of the tissue (Fig. IX, 4). The fringe of conjunctiva, which remains continuous with the bulbar part of the membrane, is raised, and a suture is passed through its margin, at a point which would be intersected by a perpendicular line let fall on to the extremity of the horizontal diameter of the cornea ; the needle is again passed through the cut edge of the tarsus at a point $6\frac{1}{2}$ mm. to one side of the suture marking the central point of the lid margin (Fig. IX, 5). A second suture is passed at corresponding points at the other side of the wound, and, when these are tied, the operation is completed. It is very important not to injure the deeper tissues when stripping off the conjunctiva and the tarsus, and to place correctly the sutures, which unite the edges of the wound. Bleeding may be troublesome occasionally, but is seldom likely to be so if adrenalin is injected with the local anæsthetic. The operation is followed by some reaction, which lasts for about thirty-six hours and then passes off quickly. The sutures may be removed on the third or fourth day, and painting with silver nitrate may be commenced at the end of the first week.

The treatment of the third stage of trachoma is chiefly concerned in the treatment of complications caused by the contraction of the fibrous tissue and by the distortion of the tarsus. The depth of the fornix is greatly diminished, partly because the membrane is shrunken, and partly because it is drawn down over the remains of the tarsus by the contracting fibrous tissue in that region, and there will therefore be less difficulty in applying drugs to its surface. Small, raised, granulating spots, which bleed easily, may be seen amongst the fibrous tissue, and the application of copper sulphate to these is beneficial. The chief indication is, however, to treat any complication, such as trichiasis, that may be present, and to recognise and to remedy any of the secondary infections that are so commonly found at this stage of the disease. The operation of excision of both fornix and tarsus is not advisable, since so little of the transitional conjunctiva remains, but much benefit may be derived from the excision of the tarsus, the diseased tissue of which often appears to serve as a reservoir of infection.

Pannus is best treated by attention to the disease of the conjunctiva, and an improvement of the corneal condition will quickly follow an improvement in the state of that membrane. A peritomy will sometimes be of advantage in helping to clear up a very vascular pannus, and a subconjunctival injection of cyanide of mercury will often hasten the disappearance of opacities. The slightly facetted, chronic ulceration, that so often persists after the conjunctiva has been practically cured, may be much benefited by the use of Scarlet R applied once or twice daily as a 2 per cent. solution in olive oil. I have also found this application to be very valuable in early cases of xerophthalmia. Dionine is often of use in promoting the absorption of opacities due to pannus. A very marked improvement in pannus nearly always follows the combined excision of tarsus and fornix. The state of the lachrymal apparatus should be carefully investigated and watched, as an infection of the canaliculi may occasionally cause a persistent corneal irritation. Jequirity is highly recommended by some surgeons for the treatment of pannus. The instillation of the drug induces a severe inflammation of the conjunctiva, and this often leads to the shrinking of the vessels which have invaded the cornea. The conjunctiva is painted every day with an infusion made from crushed jequirity seeds; the infusion is used in a 5 per cent. solution. The application is stopped when a sufficient reaction has been produced.

It is advisable for the patient to use eyedrops of $\frac{1}{2}$ per cent. solution of copper sulphate or of a 7 per cent. solution of tannic acid in glycerine for some weeks after discharge from hospital; a yellow oxide of mercury ointment should be applied at bedtime.

In conclusion, I would like to suggest that, even in apparently typical cases of trachoma, we may not be dealing with a single disease entity, and that the causes of the conjunctival changes, characteristic of trachoma, may widely vary in different cases.

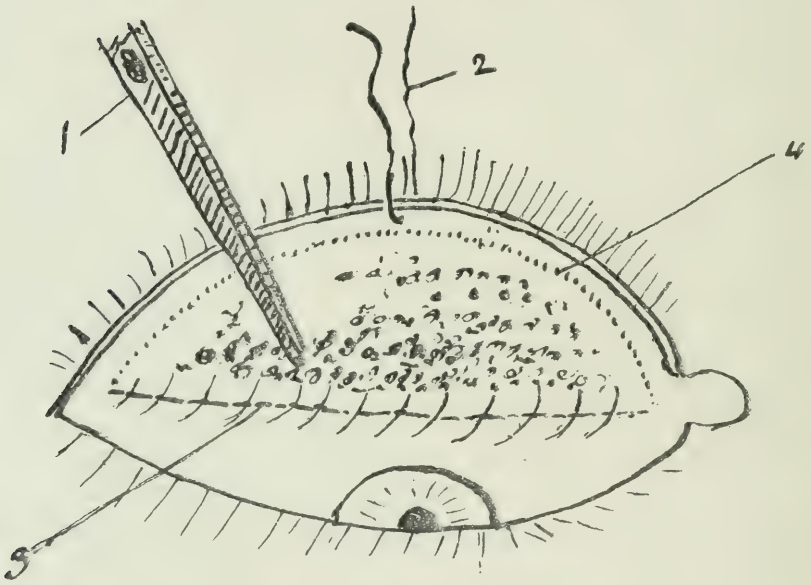


Fig. VII.

1. Fixation forceps, with catch, holding retro-tarsal fold everted.
2. Suture marking central point of lid
3. First incision, made through the transitional conjunctiva, just below the follicle-bearing area
4. Incision through tarsal conjunctiva; this is made to divide the tarsal plate in the middle portion

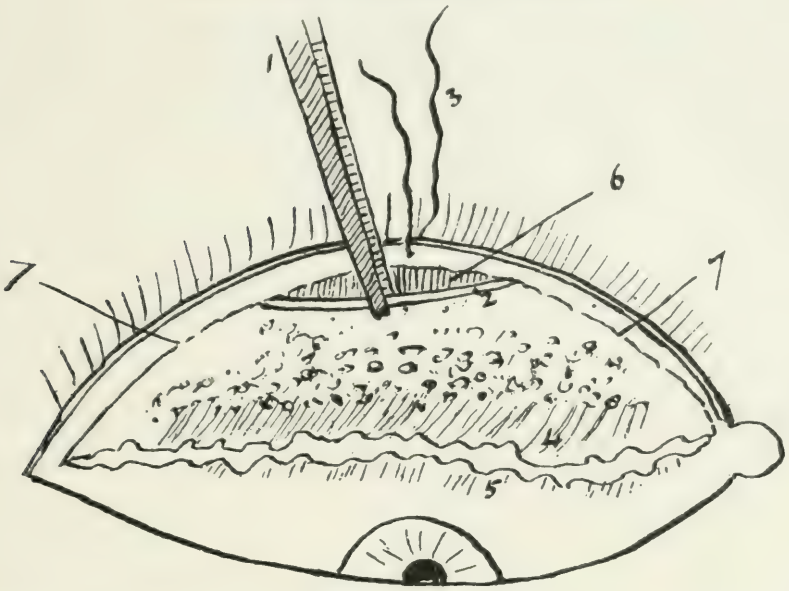


Fig. VIII.

1. Forceps gripping the edge of the divided tarsal plate.
2. Cut edge of tarsal plate.
3. Suture marking point in lid which lies over the centre of the cornea.
4. Detached fringe of transitional conjunctiva.
5. Detached fringe of bulbar conjunctiva.
6. Tissues, which underly the tarsal plate, exposed by throwing the divided portion of the tarsus downwards.
7. The incision through the tarsal conjunctiva.

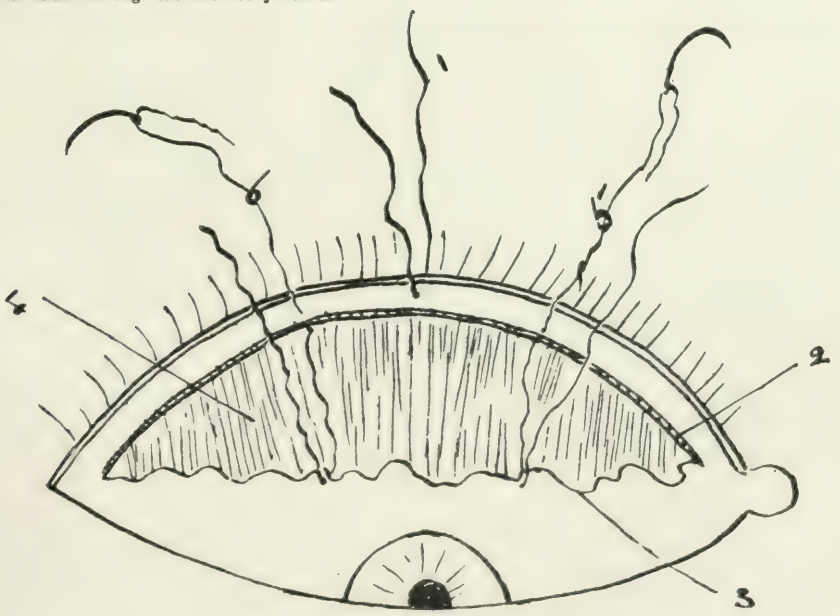


Fig. IX.

1. Suture marking the point in the lid which lies over the centre of the cornea.
2. The cut edge of the tarsal plate.
3. The cut edge of the fringe of bulbar conjunctiva.
4. Deep tissues, exposed by the removal of the tarsus and transitional conjunctiva.
5 and 6. The sutures, by which the fringe of bulbar conjunctiva is united to the cut edge of the tarsus. These are passed through the edge of the bulbar conjunctiva just to the outer side of a point which would be intersected by a perpendicular line let fall on to the extremity of the horizontal diameter of the cornea. They are passed through the cut edge of the tarsus at a point 6½mm. to one side of the suture No. 1.

Discussion.

Colonel R. H. Elliot : Colonel Kirkpatrick said that he had nothing new to tell us. If that is the case, he has certainly put before us a number of old things in a new way. One of the most important parts of his paper is his reference to the large number of conditions which, certainly in my time, we put down to trachoma. Many of the cases which we confidently called trachoma in the old days were not true trachoma. Trachoma is a word for a congeries of diseases, and not a single disease. That is a line along which some important work can be done. I should like to refer to the extraordinary importance of this question of trachoma. I am without the slightest fear of overstating the case when I say that trachoma in India, and I understand also in Persia, Afghanistan, and China as well, is responsible for more blindness than any other two factors put together. Even if you put ophthalmia neonatorum and cataract together, I do not believe that they are responsible for such a big loss of sight in Eastern countries as trachoma alone. But trachoma is, if treated properly from the first, invariably a curable disease. I have had trachoma myself, and have been completely cured of it and can speak of it from the patient's side. If a case of trachoma is treated properly from the start, blindness need never result, and yet trachoma is responsible for more blindness than anything else. It is of great importance that Governments should be awake to their responsibilities in regard to trachoma and other eye diseases. Governments—in India, for instance—have never been anything like awake enough to these diseases and to the possibility of cutting off trachoma at its earliest stages. There are two other points I would like to commend to your attention. One is Colonel Kirkpatrick's suggestion of the magnesium sulphate treatment. I have had very little opportunity of trying it myself, but I have met with a number of young men who have seen Colonel Kirkpatrick use it in Madras, and who have come back enthusiastic about its advantages. The other thing I can speak of with more emphasis, viz., the procedure of ballooning the conjunctiva. I believe that this is an extraordinarily valuable manœuvre, both from the point of view of diagnosis and of treatment.

Lieut.-Colonel S. P. James : In view of what Colonel Elliot has said about the responsibility of Governments, and the fact that trachoma in its very early stages can be treated and cured successfully, may I ask

Colonel KIRKPATRICK whether he considers that trachoma should be made compulsorily notifiable in England? That is a question we are frequently asked in the public health service.

Colonel H. KIRKPATRICK: In reply to Colonel JAMES, I am afraid my experience in England is very limited. I used to meet with a good deal of trachoma more years ago than I care to number, when I was a house surgeon in Dublin. I certainly think, however, that it ought to be notifiable. It is an infectious disease and a dangerous one, and consequently it ought to be notifiable.

Lieut.-Colonel JAMES: The difficulty is diagnosis.

Colonel KIRKPATRICK: Typical trachoma certainly should be notifiable.

Colonel ELLIOT: I should like to support Colonel KIRKPATRICK in this matter. It would be much better to have notification, even if a number of the cases turned out not to be trachoma, than to let cases of trachoma be unnotified and go far and wide. After every big war we have had numbers of cases of trachoma in this country, and, in fact, far over Europe.

TRACHOMA AMONG THE CHINESE IN FRANCE.

BY

CHARLES F. HARFORD, M.A., M.D.

The importance of trachoma from the epidemiological standpoint was clearly shown by experience gained with the Chinese Labour Corps in France, and the object lesson there afforded should lead to new efforts to definitely establish the pathology of the disease; its relation to the chronic forms of trachoma found in England; and the measures which may be adopted to stamp it out, or, at least, to minimise the serious effects which it is producing in many tropical and sub-tropical climates.

My own contact with the Chinese was but brief, but it involved certain vivid impressions which may be worthy of record, and may at least give an opportunity of emphasizing the great difficulties of diagnosis which attach to all diseases which are not identified by distinct pathological proof. I may add that during most of the time in which my observations were made I was not acting as an ophthalmic specialist, as I was doing during the greater part of my military service, but while serving in France in connection with Native Labour Corps, and mainly with those from South Africa.

1. My first touch with the Chinese was in August, 1917, when two Chinese companies arrived at Dannes to take the place of two South African companies, these being taken away by the same train which brought the Chinese. They brought no medical officer with them, and although I was appointed to a camp of South African natives about a mile away across our great ammunition dump, I was called in to help the Chinese until they obtained their own medical officer.

The immediate point which had to be considered was an ophthalmic one. The Chinese had undergone a medical inspection since landing in France, and the two companies which had been sent to Dannes were those who were regarded as suspect from the point of view of trachoma,

the companies being graded: Company A (as we may call it) being regarded as a "Trachoma Company," and Company B as a "Conjunctivitis Company." This meant that the former were regarded as potentially trachomatous, Company B, on the other hand, being composed of those who had some conjunctival trouble which rendered them suspicious.

Obviously this classification was only one of convenience, and later experience of examining large bodies of Chinese demonstrated the hopelessness of expecting exact diagnoses in such circumstances, especially when the disease itself, in its acuter manifestations at least, has no definite standard which can be regarded as wholly reliable.

As a preliminary step in dealing with these two companies the officers gave instructions for the men who were suffering from the most obvious eye troubles to be paraded for my inspection. Less than fifty were thus brought before me, and of these only a few were of any severity. The worst of these reminded me of bad cases of mucopurulent conjunctivitis seen in England, with the addition of some nodular elevations under the red velvety conjunctiva. Clearly we were faced by the presence of a form of contagious conjunctivitis which needed drastic treatment. This was rigidly carried out in this camp by a vigorous and able Canadian Medical Officer, under the instructions of Sir WILLIAM LISTER, who had visited the camp, and under the supervision of Mr. HINE, who was the ophthalmic specialist of the district. This régime will, I hope, be described by those who were concerned in its inception and execution.

2. The next problem which I was called upon to consider was the possibility of the contamination of the South African natives by their contact with the Chinese. I was able to give my opinion that the system of segregation which was well carried out by South African officers and non-commissioned officers practically excluded any danger on this ground. Certainly I have never heard of any case of trachoma arising in France among South African natives.

3. On my transference to Havre with the South African natives I was once more temporarily associated with the Chinese, when these in turn replaced the companies who were returning to South Africa.

The Chinese sent to Havre were those who had been certified as "clean" companies from the point of view of trachoma, so that the problem was a somewhat different one from that at Dannes. Our D.D.M.S., however, most wisely decided to take no risks, and a

scrupulous examination of the eyes of the Chinese was decided upon.

I paraded the company assigned to me and determined to pick out every man with red eyes, and detain all such cases for more detailed examination. I then graded these according to their severity, and had the advantage of the opinion of Mr. SICHEL, who had been recently engaged in the investigation of the causes of trachoma in Christmas Island. He gave the very decided opinion that even the few more severe cases were not of trachomatous character. He pointed out that the Chinese, with whom he was familiar, have very loose lids, that they were thus very liable to irritation and consequently accustomed to rub their eyes with dirty hands and towels, so that most of them had some congestion of the conjunctiva. I have no doubt that this was the case, and, on the one hand, it should be recognised that red eyes with these men may mean very little, and on the other hand may predispose them to worse troubles.

4. Later on in my capacity as one of the ophthalmic specialists in the Havre area, I was called upon to make a routine inspection of a large number of Chinese without any cases being found which could be regarded as suspicious.

5. Finally, I should like to bear my testimony to the excellent hospital arrangements made for the Chinese, whether at the central hospital at Noyelles or in that at Havre, in both of which Medical Missionaries from China, or those who had served as such in the past, took an important part in the work.

I am strongly of opinion (*a*) that the term trachoma is too loosely applied to cases of conjunctivitis in sub-tropical climates; (*b*) that the whole subject calls for the earnest attention of ophthalmologists and of all practitioners in these countries; and (*c*) that the governments concerned should make it the subject of searching enquiry.

AN EARLY PORTUGUESE CONTRIBUTION TO TROPICAL MEDICINE.

By CARLOS FRANÇA, Collares, Portugal.

(Translated and communicated by CLIFFORD DOBELL.)

It is impossible not to recognize the scientific character of the conquests and discoveries of the Portuguese in the fifteenth and sixteenth centuries Nevertheless, in reading treatises on tropical medicine we hardly ever meet with Portuguese names when the early history of the subject is under discussion ; though it would be surprising if the distinguished men among the Portuguese—who showed themselves, especially in Brazil, to be scientific colonists—had left no obvious traces of their activities upon tropical medicine.

Two of the historians of medicine, MAXIMIANO LEMOS and RICARDO JORGE, have noted that Portuguese physicians were the first to mention some of the tropical diseases. For instance, GARCIA DA ORTA (1583) gave a very good account of cholera ; ALEIXO D'ABREU (1623) described epidemic gangrenous rectitis (*mal do bicho**), and FERREIRA DA ROSA (1694) yellow fever. Even travellers who were not medical men gave remarkably accurate descriptions of certain diseases, and intuitively recognized the true nature of some of them. The chronicler, JOÃO DE BARROS (1552), noted the symptoms and ætiology of scurvy, from which the ship's company of VASCO DA GAMA suffered ; and another chronicler, GASPAR CORREIA, described the cholera epidemic of 1543 with admirable precision ; while the Jesuit, GASPAR AFFONSO (1596), gives one of the most complete accounts of *Dermatophilus penetrans.*†

* *Maculo* of the West Coast of Africa ; *cheringoza* of Central Africa (CAPELLO and IVENS).

† This description shows that these fleas—contrary to the statements in works on tropical pathology—existed in the sixteenth century not only in Brazil, where they were known by the name of *zungas*, but also in India, where they were called *nigoas*.

All these facts show that the Portuguese made contributions to our knowledge of the diseases of tropical countries; but not one of them appears to me so interesting as that which forms my justification for publishing the present note.

I have recently found, in a work of the sixteenth century, a very clear statement of the part played by insects in the transmission of Frambœsia tropica. In 1587 a Portuguese colonist, named GABRIEL SOARES DE SOUZA, wrote a work containing a very interesting description of Brazil, and in it may be found most complete accounts of the history, geography, and ethnography, and of the fauna and flora of our great American settlement. In this very remarkable work, which contains chapters surpassing those of PISO and MARCGRAF, I have found the following passage: "Digamos logo dos mosquitos, a que chamam nhitinga, e são muito pequenos e de feição de moscas; os quaes não mordem, mas são muito enfadonhos, porque se poem nos olhos, nos narizes, e não deixam dormir de dia no campo, se não faz vento. Estes são amigos das chagas, e chupam-lhe a peçonha que tem; e se vão pôr em qualquer cossadura de pessoa sã, deixam-lhe a peconha nella, do que se vem muitas pessoas a encher de boubas."*

The literal translation of this is as follows: "We must now refer to those mosquitoes which are called *nhitinga*, and which are very small and of the form of flies [house-flies]; these do not bite, but are very troublesome, because they settle on the eyes and in the nostrils, and will not let one sleep by day in the open, unless there be a wind. They are very fond of sores, and suck the poison which is in them; and if they then go and settle upon any abrasion on a healthy person, they leave the poison in it, and hence many people are seen covered with *boubas*."

It should be noted that *boubas* is still at the present day a popular name for frambœsia in Brazil; whilst *buba* is the Paraguayan designation for cutaneous leishmaniasis.† In the Congo, frambœsia is known

* GABRIEL SOARES DE SOUZA: *Tratado descriptivo do Brazil em* 1587. Published in *Rev. Inst. Hist. e Geogr. do Brazil*, T. XIV, 1851. The passage will be found on page 241 of this printed version.

G. SOARES DE SOUZA, who went to Bahia in 1570 and there became a planter (*roçeiro*), presented his manuscript to the Portuguese Government. Copies of it were in existence in Paris, Madrid, Portugal (Evora, Oporto, and Lisbon), in Brazil, and at Neuwied. The work was not printed till 1825, when it was published by the Royal Academy of Sciences of Lisbon. It appeared in 1851 in Brazil, through the efforts of F. A. DE VARNHAGEN.

† LUTZ, ARAUJO, and FONSECA (filho): Viagem scientifica no Rio Paraná, etc. *Mem. Inst. Oswaldo Cruz.* T.X. fasc. 2, 1918, p. 127.

under the name of *boubas* in the Kiswahili language (VAN NITSEN), and at Zumbo (Mozambique) it is called by the same name (CAPELLO and IVENS). It seems probable that the name *boubas*, and the disease to which it is applied, are both of African origin.

Although WILSON (1868) recorded that it was believed in the West Indies that framboesia is carried by flies, it is only in recent times that the conditions necessary for its transmission have begun to be understood. HIRSCH (1898) gives a description of two cases in. which the disease appeared to him to have been conveyed by flies. Both patients were living with children suffering from framboesia, and both presented "raw surfaces which could be inoculated by the poison." CADET (1897) considered that infection can only occur through pre-existent cutaneous lesions.*

But it was not until 1907 that CASTELLANI† demonstrated experimentally that flies can transmit *Treponema pertenue*. He fed a certain number of flies (*Musca domestica* and allied species) on scrapings from the slightly ulcerated papules of patients suffering from framboesia; and on examining twenty-five of these flies subsequently, he found *T. pertenue* present in preparations made from four of them. He then placed flies, contaminated in a similar manner, on the deeply scarified eyebrows of twelve monkeys, and succeeded in thus infecting three of these animals.

It would thus appear that our GABRIEL DE SOUZA clearly understood the part played by non-biting diptera in the transmission of framboesia, while he accurately defined the condition necessary for infection—the previous existence of an excoriation of the skin, upon which the fly deposits the virus. One would like to know to what little non-bloodsucking dipteran, of diurnal habits, the name *nhitinga* was applied; but I have not been able to elucidate this question.

It will be seen that GABRIEL DE SOUZA held views far in advance of his time. He might well have written, indeed, a recent chapter on the mechanism of infection, and even on the prophylaxis, of framboesia—thus

*All these authors (WILSON, HIRSCH, and CADET) are cited by Professor G. H. F. NUTTALL in "The Part played by *Musca domestica* and allied (non-biting) Flies in the Spread of Infective Diseases." *Reports of the Local Government Board on Public Health and Medical Subjects*. New series, No. 16, 1909.

†A. CASTELLANI: "Experimental investigations on Framboesia tropica (Yaws)." *Journ. Hyg.*, VII, 558, 1907.

anticipating modern views by three centuries. His name is one, therefore, which should henceforth figure in the history of tropical medicine.

Collares. *February*, 1921.

ADDENDUM.

Professor CLIFFORD DOBELL, F.R.S., to whom I wrote on discovering the passage cited above, has had the kindness to inform me that J. F. X. SIGAUD, in his work *Du Climat et des Maladies du Brésil* (Paris, 1844), refers to a manuscript which is in the Royal Library at Rio de Janeiro, and which treats of frambœsia (yaws or pian) and is dated 1587. Professor DOBELL was struck by the correspondence of the date and subject with those of DE SOUZA'S manuscript; and it is, indeed, a very curious coincidence that there should be in existence two such manuscripts dealing with frambœsia and both bearing the same date (1587). The manuscript of which SIGAUD knew, however, does not mention contagion by diptera; but it is, nevertheless, very interesting. It records how general the "mal de bobas" was among the Tupinambas, and notes the prevalence of the disease among children, and the native methods of treatment; and, furthermore, it leads one to the conclusion that frambœsia was already distinguished from syphilis towards the middle of the sixteenth century. See "*Descripção geographica da America portugueza, 1587.*" Chap. LXVII, p. 186.

A printed copy of this very rare work exists in the Public Library at Lisbon. According to some manuscript notes inserted in it, it appears that it was originally printed prior to 1811, the year of its actual publication; but its issue was suspended owing to a dispute arising between the editor—the botanist, F. J. M. DA C. VELLOSO (1742-1811)—and the Minister in charge of the Royal Stationery Office (*Regia Officina Typographica*). The original manuscript was subsequently discovered, almost complete, in the Royal Library at Rio de Janeiro.

EXTRACTS FROM THE TROPICAL DISEASES BULLETIN.

The Council has decided to publish, with the agreement of the Tropical Diseases Bureau, extracts from the *Tropical Diseases Bulletin*, not exceeding four pages in each number of the TRANSACTIONS. Colonel S. LYLE CUMMINS, C.B., C.M.G., has kindly offered to select these for publication, and the first series appears below.

MEBANE (TOM S.). **Diagnosis and Treatment of Amœbic Abscess of the Liver.**—*Jl. Amer. Med. Assoc.* 1920. Dec. 4. Vol. 75. No. 23. pp. 1566-1567.

These observations are based upon a careful study of fifty cases of liver abscess treated at the Santo Tomas Hospital, Panama, during a period of three years prior to August, 1917.

Rupture into other viscera occurred in the order of frequency into (1) the abdominal wall; (2) the subdiaphragmatic space; (3) the pleural cavity; (4) the lung, and (5) the intestinal tract. Liver abscess may give rise to several well-marked clinical pictures depending upon its location and site. The most characteristic localizing symptom is the marked tenderness elicited by tapping over the liver. Jaundice—particularly anything more than a slight scleral tinting—should be regarded as being against a diagnosis of liver abscess. Nearly all the cases showed a definite leucocytosis averaging 18,000, but varying from 12,000 to 30,000. There are cases which simulate chest conditions—usually the result of a large liver abscess located in the dome of the liver; the diagnosis may be further obscured by a pleural effusion consequent to irritation of the pleura. Usually the real condition can be detected by noting that the dulness does not follow the sinuous course of most pleural effusions—it is just in these cases that assistance can be procured from X rays.

Another type of case may simulate disease of the gall bladder, the symptoms of which are produced by an abscess on the under surface of the liver, together with secondary peritoneal adhesions.

The high mortality, more than a third, in the present series of cases could be ascribed to the poor condition of the patients on admission. As a means of arriving at earlier diagnosis—so very important—the more extended use of hepatic puncture is recommended. As a matter of precaution all punctures were made in the operating room with the patient prepared for operation. When pus was found immediate operation was performed. When possible, the transthoracic method of approach is to be preferred, the direction of the needle of the successful exploratory puncture being taken as a guide. When approach through the chest is impossible, a rectus, or Kocher gall-bladder, incision may be employed. P. H. M.-B.

STOKES (ADRIAN) & BIGGER (J. W.). **A Short Account of Dysentery in Dublin in the Autumn of 1919.**—*Dublin Jl. of Med. Sci.* 1920. Mar. Fourth Series. No. 1. pp. 3-8.

In August, 1919, an epidemic of bacillary dysentery, the first recorded in modern times, broke out in Dublin. In all, 186 cases with 19 deaths were notified. The

pathological anatomy in the autopsies was characteristic of bacillary dysentery. Out of 139 patients, whose fæces were examined bacteriologically, the dysentery bacillus was isolated in 76, or in 59·6 per cent. The majority were Shiga infections ; Flexner's bacillus was encountered once only. Serological reactions were found to be most regular ; the highest titre with the homologous organisms being 1 : 80. No difficulty was experienced in isolating or identifying the organisms, and a rough method of preliminary agglutination of the colonies with specific antiserum was employed.

P. H. M.-B.

KIRSCHNER (L.) & SEGALL. **Zur Bakteriologie der Ruhrerkrankungen des Jahres 1920 in Wien.**—*Wien. Klin. Woch.* 1920. Dec. 23. Vol. 33. No. 52. pp. 1125–1126.

The experience of the authors was gained in the 1920 epidemic of bacillary dysentery in Vienna. Impressed with their failure to isolate dysentery bacilli from a large number of fæcal specimens when transmitted to the laboratory, as well as by reports of FRIEDEMANN, who claims to have obtained positive results in 100 per cent. of his cases by means of rectoscopic culture [see this *Bulletin*, Vol. 11, p. 259], they decided to give the latter method a trial. From stools transmitted to the laboratory positive results were recorded in only 6 per cent. ; from freshly passed fæces cultured in hospital the figure was 39 per cent. ; while from mucus obtained by the proctoscope successful isolations were recorded in 65 per cent. Examples of the more familiar types of dysentery bacilli—Shiga, Flexner Y, Strong's bacillus—and also in certain cases SCHMITZ'S recently described type were recognised. They also suggest that *Bacillus fæcalis alcaligenes* plays a rôle in producing dysenteric symptoms.

P. H. M.-B.

RELE (V. G.) **Incidence of Sprue in Bombay, its Pathology and Treatment. A Paper read before the Bombay Medical Union on Jan. 16, 1920.**—37 pp. Bombay. 1920. Printed at the Bombay Vaibhav Press. [Price Two Rupees.]

The author has contrived to say a good deal about sprue in a reasonably short space. It is impossible to obtain exact statistics about the mortality in sprue in a city such as Bombay, where the monthly mortality from all causes is about 2,500. The disease, however, has assumed a position of considerable importance in this city, for which the climate and conditions of life are held to be responsible. Sprue is usually a disease of mature years, being common between the ages of 25 to 50, and is rarely seen in children. It is commoner in women than in men ; in fact, women in Bombay, according to the author's experience, have a higher ratio of mortality from intestinal diseases of all kinds than have men.

The endemicity of sprue in Bombay is not held to be due directly to climatic conditions, because in other towns of the Presidency similarly located the disease is by no means so common, nor can it be held to be due to the food, as other communities, who live on exactly the same dietary, escape. Though sprue cannot be said to originate in unsanitary conditions, it finds a very congenial soil in places where drainage is neglected. The author is inclined to believe that sprue is nothing but a biological manifestation and final stage in the progress of dyspeptic trouble, and is the result of prolonged over-secretion by the stomach and duodenal glands.

The occurrence of one or more cases in the same family leads one to suppose that infection from one sprue case to another is possible. The symptoms of sprue group themselves into three stages :—

First stage, oral and dyspeptic troubles.

Second stage, intestinal symptoms.

Third stage, toxæmia, inanition, and anæmia.

Sprue may be grafted upon acute bacillary dysentery, or any other intestinal complaint, and in that case may prove fatal in a very short time.

The section on the pathology is purely speculative. It is thought that all the

changes observed in sprue hinge upon the deficient production of secretin. Deficiency of this substance leads to a lowered activity of the pancreas, with consequent deficient digestion and mal-assimilation of food.

With reference to treatment, he is by no means confident that chromosantonin, as advocated by BEGG, justifies the claims made for it. In his practice he considers that in one case the drug was responsible for a smart intestinal hæmorrhage, and in a second for acute jaundice with high fever. Emetine injections are stigmatized "as a waste of a good remedy for what it is not meant." A milk dietary in Bombay being unsatisfactory, recourse should be had to treatment with buttermilk. One teaspoonful of curds is added to 26 oz. of milk previously boiled and cooled. After curdling it is churned and water added. The fat must be removed from the curdled milk, and churning should not be considered complete until this has been effected. The resulting butter-milk is given in much the same manner as the milk treatment is usually arranged. The patient is told to take 38 oz. of milk a day for curdling, and the next morning is instructed to take his first cup at 7 a.m. and the remaining quantity he is to finish before 3 p.m. After that time he is to take the milk prepared from that set aside early in the morning of the same day, and so on. During the night-time nothing but water is drunk. The idea is that, if kept more than six hours on a hot day, the butter-milk may turn sour. The amount is gradually increased, so that he is taking 70 oz. on the fifth day; finally, the maximum quantity in the 24 days should be 140 oz. (or seven pints). A pinch of table salt to a cupful of this milk greatly improves the taste. It is not possible to keep the patient on a regimen of this sort for more than two or three weeks, after which the addition of fruit is advisable. There are better fruits in Bombay than strawberries, which are very expensive. The following are recommended: pomegranates, sweet lemons (Santra), oranges, bananas, papaya, mangoes, apples, pineapples, peaches, pumelo, and musk melon. Pomegranates are specially recommended, and next to these bananas—whether dubbed locally "plantain" or "banana" does not signify as long as they are ripe. Some patients do well on mango juice. Although most cases do well on the butter-milk diet, there is a group which is in no way benefited. They go on losing in weight, and the doctor is blamed for starving them; these are hopeless cases, beyond the range of any form of treatment.

The author does not consider a change of climate necessary as long as the patient carries out the treatment effectively at his place of residence. The seaside is better than the hill station for sprue convalescents in India. A good rule to observe is to send patients away from the endemic area to places where the mortality from diarrhœa and dysentery is lowest. P. H. M.-B.

CONRAN (PHILIP). **Meat Diet in Sprue.**—*Brit. Med. Jl.* 1920. Aug. 7. pp. 206—207. With one chart.

A pure meat diet, almost the complete antithesis to milk regime, is occasionally of value in the most advanced and chronic stages of sprue. Two cases illustrating the advantages of this method of treatment are cited in the paper under review. The first case contracted sprue in India. At the beginning of 1919 she weighed only 5 stone 8¾ lbs., and presented signs and symptoms of an advanced stage of the disease; there was considerable anæmia. Test meals showed that there was general delay of digestion and assimilation throughout the intestinal tract. Meat diet consisted of 1 lb. 9 oz. of minced beef daily, pressed into cake and lightly cooked with 2 oz. of suet, and taken as five meals of 5 oz. each. After a few days the quantity was increased to 1 lb. 14 oz., given in five meals of 6 oz. each; hot water being sipped between each feed.

Subsequently this diet was considerably amplified by the addition of strawberries, egg-flip, bananas, rusks, etc., and in the nineteenth week the number of meals was reduced to four daily.

The dietetic treatment was supplemented by intestinal lavage, which proved of

value in relieving the irritation of the lower bowel; in the later stages massage and the faradic current helped to restore the muscular tone of the abdominal wall.

During the first few weeks the weight dropped, and tetany of the hands and arms supervened. Medicinal treatment was for the most part symptomatic, chromosantonin grs. 5, twice daily, as recommended by BEGG, having little, if any, apparent effect. Improvement on meat diet was striking; the blood circulation first showed improvement; then the stools. In the last four weeks of the patient's stay at Duff House the average total day weight of fæces was 89 grammes, and over 4,000 calories of food were being taken.

On leaving the institution the patient had put on 2 stone 12¾ lb., and the bowels were opened naturally and regularly once a day on an approximately normal diet.

The second case, also a woman, contracted her illness originally in the West Indies, and gave a history of having suffered from two attacks of tetany in 1917. On admission her weight was 5 stone 12½ lb., together with considerable anæmia and the more familiar symptoms. The absorption of fat and protein was found to be deficient. With the introduction of an exclusive meat diet definite improvement began; the attacks of tetany ceased, and the condition of the mouth became normal. She was discharged from Duff House after eleven months' residence, and after having gained 1 stone 8¼ lb. in weight since admission. P. H. M.-B.

HEATON (TREVOR). **The Etiology of Sprue.**—*Indian Jl. Med. Res.* 1920. Apr. Vol. 7. No. 4. pp. 810–839.

This is a well-considered compilation originally submitted as a thesis to Oxford University in 1919.

It contains few original observations on the disease, but the information is well arranged.

The following are the conclusions drawn:—

Sprue is a definite entity, and not a mere association of symptoms. Its predisposing and complicating factors lead to, or depend upon, a single pathological condition.

There is no positive evidence to suggest that this is a specific bacterial or protozoal infection. These organisms may be present, and their destruction may be necessary for the cure of the disease; but sprue symptoms may exist in their absence.

The symptoms of sprue are due mainly to two factors, namely, mycotic fermentation and digestive incompetence. The two most probable theories of the disease are accordingly that it is a mycosis, or that it is a physiological exhaustion-state due to climate. Whichever of these be the primary, they operate in a vicious circle. Defective digestion favours the multiplication of organisms, while an infective catarrh accentuates digestive weakness.

The peculiarities of the incidence and geographical distribution of sprue point to a physiological rather than an infective cause.

The immediate relief from all infective systems in response to non-specific treatment is contrasted with the very slow and uncertain recovery of the digestive function. This is also taken to indicate that the digestive failure is the essential disability, and the infection secondary.

The prominence of infective processes in the mouth in most sprue cases, and their tendency to relapse, cannot be explained by any theories of physiological failure of digestion. It is, however, less easily explicable by any infective hypothesis, for it is in origin physiological, depending essentially upon a condition of lowered resistance; the actual infecting organism being accidental.

The physiological disability of sprue is brought about by the effects of climate. In cœliac disease of children a similar disability is present, but it is congenital.

Hill diarrhœa is essentially a form of sprue, acute in onset and uncomplicated in course; the disease affords an example of sprue symptoms arising in the absence of infective causes. The physiological fault underlying these three diseases may lie in the actual digestive glands themselves, the liver and pancreas. Possibly, however, it may be that the supply of the chemical ferment secretin is deficient, thereby depriving these glands of their normal stimulus. P. H. M.-B.

LIST OF FELLOWS.

The following have been duly elected Fellows of the Society:—

March 18th :—

Henry Joshua Augustine, L.R.C.P. & S. (Edin.), D.T.M. (Liverpool), 16, Chalfont Avenue, Wembley.

Harry Arnold Baylis, M.A. (Oxon.), British Museum (Natural History).

Major Frederick T. G. Hobday, C.M.G., F.R.C.V.S., F.R.S.E., 6, Berkeley Gardens, Kensington, W.

Major Robert Forrester D. Macgregor, I.M.S., M.B., Ch.B. (Edin.), Sistan, India.

Albert Rutherford Paterson, M.B., Ch.B. (Glas.), D.P.H. (Cantab.), Nairobi, Kenya.

May 20th :—

Osman Mohammad Banhawy (Egyptian Medical Diploma), Cairo.

John Osmonde Beven, M.A. (Cantab.), M.R.C.S. (Eng.), L.R.C.P. (Lond.) Colonial Medical Service, Kenya Colony, B.E.A.

Shankar Sakharam Bhagvat, M.B., B.S., L.M., Bombay.

John Bramley-Moore, L.M.S.S.A., British North Borneo.

Philip Norman Button, O.B.E., M.R.C.S. (Lond.), L.R.C.P., Surgeon-Lieut.-Commander, R.N., c/o Admiralty, S.W. 1.

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Cheng Kun Chen, M.B., B.S., Swatow, China.

Johannes Cornelius Coetzee, M.B., B.Ch., B.A.O., L.M. (Ireland, Dublin University), Adelaide, S. Africa.

Francis Xavier Costello, L.R.C.P., L.R.C.S., L.D.S. (Ire.), c/o Williams Deacon's Bank, 2, Cockspur Street, W.

Andrew Crawford, M.B.E., L.R.C.P.E., L.R.C.S.E., L.R.F.P.S.G., L.D.S. (Glas.), c/o Principal Medical Officer, Accra, Gold Coast Colony, West Africa.

Kaikhooshro Ardesheer Gandhi, M.B., B.S. (Bombay), D.P.H. (Lond.), Bombay.

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Arnold Roland McLean, M.B., Ch.B. (Edin.), Trinidad.

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Bt.-Lieut.-Col. Arthur Olver, C.B.. C.M.G., R.A.V.C., F.R.C.V.S., c/o Holt & Co., 3, Whitehall Place, S.W. 1.

Parasurama Parthasarathy, L.M. & S., B.S.Sc. (Madras), L.R.C.P. & S. (Edin.), Bangalore, India.

Thomas Edmund Rice, C.M.G., L.S.A., D.P.H., R.C.S. (Ire.), Lagos.

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Major Henry Edward Sutherland Richards, M.D., B.Ch., R.U.I., R.A.M.C. (T.F.), St. Lucia.

Cyril Randolph Wallace, L.R.C.S., L.R.C.P., L.M. (Ire.), Arusha, Tanganyika Territory.

James Montague Wallace, M.A., M.R.C.S., L.R.C.P., Wendela, Sudbury Hill, Harrow, Middlesex.

Alfred Annesley Woods, L.R.C.P. & S.I., D.P.H., Malay States.

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